the anterior olfactory lobe of the guinea pig

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the anterior olfactor

a descriptive and experimental anatomical study

PROMOTOR: PROF. DR. H. J. LAMMERS

obe of the guinea pig

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voor To

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General Introduction

The following study was undertaken as an experimental morphological investigation into the secondary olfactory connections in the guinea pig with the help of a silver impregnation method

Whereas earlier investigations in this field were made with the atrophy method or with the Marchi impregnation, there have appeared from 1947 onwards various studies on the olfactory connections in other mammals than guinea pigs, in which silver impregnation methods were made use of

For our research we chose the silver staining methods of Nauta (1950, 1957) and of Nauta and Gygax (1954) With these techniques not only preterminal degeneration can be shown, but also degeneration of the stem fibres Moreover, the first method is also suited for paraffin sections

As a second histological technique to show degenerated fibres we used the combined myelin and cell impregnation of Kluver and Barrera (1953)

The efferent connections of the olfactory bulb were examined by making, mostly small, surgical and electrolytic lesions There it appeared that, if the lesions were confined to the rostral part of the olfactory bulb, degenerated fibres could be found in the lateral olfactory tract only If the lesions were situated more caudally in the olfactory bulb or at the transition from the bulb to the olfactory peduncle, degenerated fibres were also found in the anterior limb of the anterior commissure

This observation led us to draw into our study the origin and termination of this part of the anterior commissure, to which end lesions were made in the remaining areas of the anterior olfactory lobe

Doing this we found that also the medial forebrain bundle takes part in the projection of the anterior olfactory nucleus

Apart from the rather concise descriptions by Rose (1912) and Johnson (1957 a), we had in order to define precisely the positions of the lesions made and to determine the course and termination of degenerating fibres, no other data about the nuclear structure of the anterior olfactory lobe in the guinea pig than descriptions of this area in closely related mammals

For this reason we made a supplementary study of the cytoarchitectonics of the anterior olfactory lobe in the guinea pig

The nuclear configuration of the anterior olfactory lobe

In the anterior olfactory lobe of the guinea pig the following areas may be distinguished (cf the classification of Gastaut and Hammers, 1961, for man)

1 Area bulbaris
   - a bulbus olfactorius
   - b bulbus olfactorius accessorius

2 Area retrobulbaris s pedunculus olfactorius
   Nucleus olfactorius anterior

3 Cortex praepiriformis

4 Area olfactoria
   - a tuberculum olfactorium
   - b substantia perforata anterior
   - c gyrus diagonalis

5 Area septalis

The amygdaloid complex together with the periamygdaloid cortex and the entorhinal and presubicular cortices constitute the lobus olfactorius posterior s lobus piriformis

The anterior olfactory area has been entirely or partly described in many mammals in Ornithorhynchus by Elliot Smith (1895, 1896) and Hines (1929), in Didelphys by Herrick (1924) and Loo (1931), in Caenolestes and Orolestes by Obenchain (1925), in the mole by Ganser (1882) and Johnson (1957 b), in Soricidae and Galago demidovii by Andy and

Stephan (1962, 1959), in the bat by Humphrey (1936) and Mann (1961), in Orycteropus by Sonntag and Woollard (1925), in the mouse by Rose (1929) and O'Leary (1937), in the rat by Craigie (1925), Gurdjian (1925) and Kreiner (1934, 1937), in the guinea pig by Johnson (1957 a), in the canadian beaver by Pilleri (1961 a, d), in the rabbit by Winkler and Potter (1911), Rose (1931) and Young (1936), in the cat by Winkler and Potter (1914) and Fox (1940); in the mink by Jeserich (1945), in the panda by Lauer (1949), in the porpoise by Breathnach (1953), in Macacus by Lauer (1945), and in man by Crosby and Humphrey (1938 b, 1941), Allison (1954) and Landau (1958)

Discussing the anterior olfactory lobe in the guinea pig we confined ourselves to comparisons with the corresponding area of closely related mammals An extensive phylogenetic discussion would be beyond the scope of this monograph

In this connection reference is made to the studies by Cajal (1901, 1902, 1911, 1955), Beccari (1910), Rose (1912, 1926, 1927), Johnston (1913, 1923 a, b), Ariens Kappers, Huber and Crosby (1936), Crosby and Humphrey (1938 a, 1939 a, b), Allison (1953 b), Foroglou (1959), and Gastaut and Lammers (1961)

Material and methods

Four adult and four young (11 and 24 days old) guinea pigs (Cavia porcellus) were utilized for this study

The animals were perfused under nembutal anaesthesia with 10% formol-saline (60 ml per kg of bodyweight) After at least six hours the brains were removed from the skulls

We allowed this interval to elope as, according to Droogleever Fortuyn (1927) and Cammermeyer (1961), shortly after death shrinking of the cells may occur as a result of mechanical influence on the tissue After four to six hours the cells would definitely be dead and not react by shrinking

After preserving in 10% formalin for some weeks, the brains were embedded in paraffin and serially sectioned either in frontal, horizontal or sagittal planes The sections (10 or 15 μ) were stained with cresyl violet and by the Kluver-Barrera technique (1953)

The serial drawings of the frontal and horizontal sections were made respectively from the brains of an 11 and 24 days old animal The brains of these young animals showed no essential difference in cytoarchitecture with the brains of adult animals

All photomicrographs were made from adult animals

Area bulbaris

Bulbus olfactorius

The olfactory bulb in the guinea pig consists of the following layers from without inwards (fig 1):

1 Stratum fibrorum, a layer of non-myelinated nerve fibres of the nervus olfactorius This layer is very thin on the dorsal side of the olfactory bulb

2 Stratum glomerulare This lamina consists of one, occasionally two rows of glomeruli, circumscribed islands of grey matter, surrounded by small stellate elements These periglo-

merular or external granular cells (fig. 45, A 1) exhibit in the Nissl impregnation only a thin rim of hard-staining Nissl substance round a nucleus, which is poor in chromatine and has a dark nucleolus.

According to various authors the external granular cells form beneath the stratum glomerulare the stratum granulare externum.

Fig. 1. Photomicrograph of frontal section through the rostral third of the olfactory bulb. Klüver-Barrera method. Magnification 45

Pilleri (1961 a) reports that in Castor canadensis and various other mammals the glomeruli are surrounded by dense capsules of glia cells, in which only a few nerve cells are to be found, mostly one and never more than two per glomerulus. This author considers these "cellule nervose piccole" of Golgi to be the same as the "grains externes", the external granular cells of Cajal. Considering the small number of these cells we may assume however that they are interstitial tufted cells. The external granular cells are in our opinion wrongly described by Pilleri as glia cells. In the guinea pig only a few glia cells are found in the glomerular layer.

3. Stratum plexiforme externum or stratum moleculare. In this layer are found the tufted cells (cellules à houppette, cellules à panache of Cajal). These cells correspond with the "cellule nervose grandi" of Golgi (Pilleri, 1961 a).

They are medium-sized cells of variable shape and with darkly staining Nissl substance. According to their position they may be subdivided into: internal tufted cells (fig. 45, A 2)

lying in the plexiform layer, external tufted cells in the periphery of the plexiform layer extending to the vicinity of the glomeruli, and interstitial tufted cells (fig 45, A 1) between the glomeruli The size of the cells decreases from within outwards In the guinea pig the external type is predominant

4 Stratum mitrale or stratum granulosopyramidale This layer consists of

a) granular cells, small, closely packed, cells with little or no demonstrable Nissl substance The cells derive their name from the resemblance to the elements of the granular layer of the cerebellum (Gehuchten and Martin, 1891)

b) mitral cells (cellules mitrales), very large cells with darkly staining Nissl substance and a predominantly round nucleus (fig 45, A 3) They are situated at various levels and may also be lying more peripherally in the stratum plexiforme externum or more centrally in the stratum granulare

Crosby and Humphrey (1939 a, b), who describe the olfactory bulb in a great number of vertebrates, do not distinguish mitral and tufted cells The tufted cells, described above, are regarded by them as displaced mitral cells

5 Stratum plexiforme internum Just as in the cat (Fox, 1940), this lamina cannot clearly be distinguished as a separate layer in most places, because of the frequent occurrence of granular cells

6 Stratum granulare The inner granular cell layer consists of islands of closely packed granular cells, which form several layers

Among these cells there occur, beside displaced mitral cells, cells that resemble the neurons of the pars rostralis of the anterior olfactory nucleus as regards shape and size They are the same cells as the "cellules a cylindre-axe court ' (short-axon cells) of Cajal (1911) and the "cellules étoilees" of Allison (1953, a) These cells are also described by Pilleri (1961, a) In the description of the olfactory bulb in the guinea pig by Johnson (1957, a) the cells are not mentioned, although they can be recognized very clearly with the Nissl impregnation

7 Stratum periventriculare This layer consists of small ependymal cells and some short-axon cells

At the transition from the bulb to the olfactory peduncle the olfactory formation terminates first on the dorsal and ventral side On the ventromedial side it continues farthest caudally

As the fibres that are going to form the lateral olfactory tract shift laterally in the posterior part of the bulbar area, the outer layers of the olfactory bulb disappear except the stratum granulare This layer, which is now situated on the medial side of the tract, blends caudally with the pars externa of the anterior olfactory nucleus

Bulbus olfactorius accessorius

The accessory olfactory bulb, also called accessory bulbar formation or bulbus parolfactorius, is extremely well developed in the guinea pig (Cajal, 1902) It forms an hemispherical non-prominent structure on the dorsolateral side of the olfactory bulb, of which it occupies the posterior part On the dorsal side the accessory bulb is overlapped by the cerebral hemisphere

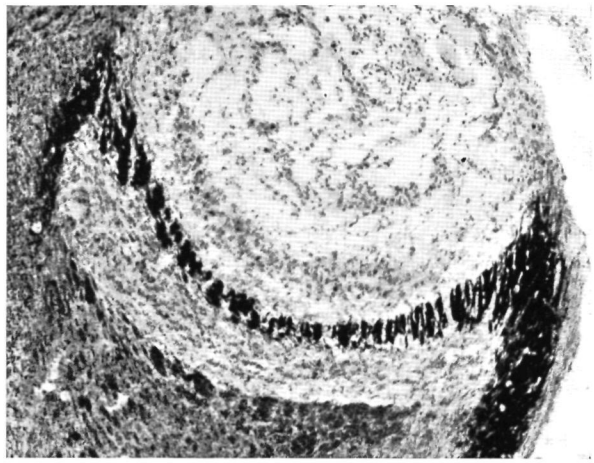


Fig. 2. Photomicrograph of frontal section through the middle third of the accessory olfactory bulb. Klüver-Barrera method. Magnification 45X

The following layers may be distinguished (fig. 2):

1. Stratum fibrorum. This layer is made up of non-myelinated nerve fibres from the organon vomeronasale, which enter the accessory olfactory bulb at the lateral side (McCotter, 1912).
2. Stratum glomerulare. The glomeruli are less definitely circumscribed than those in the olfactory bulb.

In the guinea pig, just as in the cat (Fox, 1940) and the rabbit (Allison, 1953 a, b), the periglomerular cells are fewer in number than in the olfactory bulb. As in the olfactory bulb, some students report a stratum granulare externum.

3. Stratum plexiforme externum, an area with few cells.
4. Stratum mitrale. Beside a few granular cells, this layer consists of four to five rows of medium-sized cells (fig. 45, B 1) with predominantly oval nuclei and darkly staining Nissl substance. Some cells are found in the outer and inner plexiform layers.

As regards shape, size and distribution of Nissl substance they resemble the internal tufted cells of the olfactory bulb. While Allison (1953, b) calls them mitral cells, Cajal (1955) reports: "None of the cells has the shape, size or regularity of position and alignment of the bulbar mitral cells. One may thus say that the accessory lobule lacks mitral cells."

5. Stratum plexiforme internum, an area with few cells. This layer is as wide as the outer plexiform layer.
6. Stratum granulare. The granular cell layer of the accessory olfactory bulb is made up of several rows of granular cells, more compactly arranged than those in the main bulb. The layer is not a continuation of the granular cell layer of the olfactory bulb. Moreover, short-axon cells do not occur.

Just below the internal plexiform layer the granular cell layer is traversed by deeply

myelinated nerve fibres, which pass from the dorsal side of the olfactory bulb to the lateral olfactory tract Young takes the layers, that are situated central to these fibres, to belong to the pars dorsalis of the anterior olfactory nucleus (cf Young, 1936, fig 3 of the rabbit and fig 18 of the guinea pig)

According to Gurdjian (1925) the stratum granulare is completely lacking in the albino rat Rose (1929, 1931) takes only the strata fibrorum, glomerulare and granulare as belonging to the accessory olfactory bulb The stratum mitrale is regarded by him as a regio retrobulbaris of the accessory olfactory bulb

Area retrobulbaris

The retrobulbar area is occupied by the nucleus olfactorius anterior This nucleus has a variable extension, especially at its rostral end As this part of the anterior olfactory nucleus is situated intrabulbarly and at the transition from the olfactory bulb to the retrobulbar area — in which area many lesions were made in our experiments — we paid special attention to this

After a description of the anterior olfactory nucleus of an 11 days old guinea pig, a survey is given of the variability of the rostral part of the nucleus, followed by a discussion

The nucleus olfactorius anterior of an 11 days old guinea pig

Rostrally the anterior olfactory nucleus makes its appearance in the bulbar area as two cell groups beneath the rostral tip of the accessory olfactory bulb (fig 6) a medial cell group lying right medial to the granular cell layer of the accessory bulb, and a lateral cell group lying laterally beneath the granular cell layer Both groups consist of medium-sized neurons (fig 45, B 2) with round or oval nuclei and darkly staining Nissl substance The medial cell group appears a little more rostrally and is slightly larger than the lateral one

We have called these cell groups the pars rostralis of the anterior olfactory nucleus The rest of the anterior nucleus has no contact with these cell groups and is seen first at the level of the posterior third of the accessory bulb (fig 8) At this plane the olfactory formation of the main bulb is only present on the ventral and medial sides Lateral and dorsomedial to the olfactory ventricle cell conglomerations appear, the cells of which resemble those of the pars rostralis Farther caudalward these cell groups become larger, extend dorsally and join each other The nucleus also extends ventrally around the ventricle When the bulbar and accessory bulbar formations have disappeared, the ventricle of the olfactory peduncle is completely surrounded by the anterior olfactory nucleus (fig 9)

At this level the nucleus may now be divided into a pars dorsalis (figs 8, 9), lying dorsomedially, and into a pars lateralis (figs 8-11) A clearly defined pars ventralis is not yet present, while the pars medialis appears more caudally, when the pars dorsalis has merged into the frontal cortex

These various portions of the anterior olfactory nucleus of the guinea pig can be distinguished not only by their topographical location, but there are also certain differences in cell type and arrangement

The pars medialis (figs 10-14) has a more compact outer and a less compact inner cell layer Externally the transition to the frontal neocortex is still indicated along a short distance

by a fissure (mentioned by Winkler and Potter in the rabbit as incisura rhinica, in the cat as sulcus rhinalis medialis) We have named this fissure in the guinea pig fissura rhinalis medialis (fig 10)

In the pars ventralis (figs 10-13) there occurs no lamination This part of the anterior olfactory nucleus is characterized by its slightly smaller cells (fig 45, C 2), the irregularly serrated transition of its cell layer into the plexiform layer, and the radial arrangement of its cell layer in the ventromedial angle of the hemisphere

The pars lateralis exhibits a homogenous cell layer, which is less compact at the level of the pars externa as a result of the fibres running from the anterior commissure to this mainly laterally situated cell group (Kreiner, 1937)

Near the region, in which the olfactory ventricle becomes continuous with the lateral ventricle the pars ventralis extends dorsally and constitutes a pars posterior (figs 12, 13), which is caudally separated from the nucleus accumbens by a plexiform layer The cells of the nucleus olfactorius anterior pars posterior (fig 45, C 3) are of the same size as those of the other portions of the anterior nucleus (fig 45, B 2-C 1), except the pars ventralis (fig 45, C 2) and the pars externa (fig 45, D 1)

Followed caudalward the pars ventralis of the anterior olfactory nucleus is continued in the olfactory tubercle and the homogeneous cell layer of the pars lateralis is gradually replaced by the two cell layers of the prepiriform cortex The pars medialis continues farthest caudalward (fig 14) At the rostral tip of the olfactory tubercle this portion of the anterior nucleus shifts dorsocaudalward and becomes continuous with the precommissural hippocampus or nucleus hippocampi anterior, which can be regarded as a rostroventral continuation of the indusium griseum (fig 4) The cells of this nucleus (fig 46, A 3) have a more darkly stained Nissl substance and are more compactly arranged than the cells of the superficial part of the pars medialis (fig 45, C 1)

The pars externa of the anterior olfactory nucleus is first seen rostrally, as a compact group of small neurons (fig 45, D 1) with little Nissl substance, laterally in the posterior part of the olfactory bulb between the nucleus olfactorius anterior pars lateralis and the lateral olfactory tract (fig 8)

This cell group does not extend rostrally as far as the pars lateralis Dorsally the pars externa is bounded by the stratum granulare of the accessory olfactory bulb, while ventrally at this level granular cells of the main olfactory bulb are still present

More caudally, as the granular cells of the bulbar and accessory bulbar formation disappear, the pars externa extends ventrally and dorsomedially Another group of cells appears dorsomedially and becomes dorsally continuous with the former cell group just caudal to the accessory olfactory bulb

After this coherence has broken up, the pars externa extends medially and laterally in the olfactory peduncle as two cell columns (figs 9-11), which gradually shift in ventral direction, but do not meet These crura of the pars externa are no continuous cell groups, but exhibit many gaps, especially medially The crus mediale extends as far caudalward as the caudal third of the pars dorsalis of the anterior olfactory nucleus, the crus laterale extends as far as the rostral extreme of the pars posterior

The position and arrangement of the different portions of the anterior olfactory nucleus is also clearly demonstrated in the drawings of the horizontal sections of the brain of a 24 days old guinea pig (fig 25-30)

Pars rostralis

While examining several series of guinea pig brains there appeared to be a great variability in the number and size of the cell clusters of the pars rostralis, in their position and in the coherence with the rest of the anterior olfactory nucleus This variability does not only exist between different brains, but also between the right and left pars rostralis of one guinea pig brain

For the sake of a closer examination of this the brains of thirty young and adult, normal and operated, guinea pigs were sectioned serially (6 frontally, 20 horizontally, 4 sagittally), 10 or 15 μ Every fifth, sometimes every third section, of the bulbar and retrobulbar area was stained according to the method of Kluver and Barrera

The varying appearance of the pars rostralis may best be demonstrated in the horizontal series The sections of these series are numbered from dorsal to ventral, those of the sagittal series from lateral to medial

Series 320, right side (fig 35) The pars rostralis consists of a large cell group lying medially beneath the granular cell layer of the accessory olfactory bulb (466) and of a more ventrally lying lateral cell group consisting of only a few cells (501)

Series 333, right side (fig 36) The pars rostralis consists of only one cell group, lying dorsally in the olfactory bulb

Series 353, right side (fig 37) Several cell groups are present A medial cell group is found dorsally in the olfactory bulb (516) More ventrally lies another medial cell group (524) and a lateral group of cells (531) The second medial cell group extends farthest ventralward (546)

Series 325, right side (fig 38) Here too, the pars rostralis consists of several cell clusters Dorsally in the bulbar area a medial and a lateral group of cells are present (286) The lateral cell group has disappeared a few sections more ventrally (299) Another medial and lateral cell group are only found in a few sections (315), while the first medial cell group continues farthest ventralward (331) In front of the dorsal part of the pars externa a cell group appears (340), which is really part of the anterior olfactory nucleus pars dorsalis (345)

Series 322, right side (fig 39) Beside a medial cell group (625) and a lateral cell group (655), small cell conglomerations are present in the centre of the olfactory bulb Its cells have the same aspect as those of the pars rostralis Discussing the structure of the olfactory bulb we already drew attention to the presence of these cells in the periventricular gray

Series 319, right side (fig 40) In contrast with the previous series, in which the cells of the pars rostralis are not continuous with the rest of the anterior olfactory nucleus, the lateral cell group of the pars rostralis in this guinea pig constitutes a dorsal extension of the anterior end of the pars lateralis (360, 370, 390) The medial cell cluster is an independent group of cells (320)

Series 319, left side (fig 41) The pars rostralis consists of two cell groups lying dorsally in the olfactory bulb (310) More ventrally lies a third cell group (370), which becomes continuous with the pars lateralis of the anterior olfactory nucleus (390)

Series 329, left side (fig 42) In this brain it is not the lateral but the medial cell group of the pars rostralis, which is continuous with the rest of the anterior olfactory nucleus (390, 400) The cell groups of the right olfactory bulb (fig 43) have no such contact

Series 378, right side (fig 44) The pars rostralis consists of a medial (690) and a lateral cell group (670, 660) The medial cell group is connected with the rest of the anterior olfactory nucleus by a few cells

From these data it is apparent that the cell clusters, which constitute the pars rostralis of the anterior olfactory nucleus, do occur in variable size, number and position Mostly two cell groups are present, a medial and a lateral one, which lie separated from the other portions of the anterior nucleus In some brains, however, the cell groups are continuous with the pars lateralis or pars dorsalis There may also exist differences in appearance between the right and left pars rostralis of one guinea pig brain

Discussion

The name "anterior olfactory nucleus" for the cell group lying in the olfactory peduncle has been introduced by Herrick (1910) in his study of the forebrains of amphibians and reptiles As regards mammals the nucleus as such was first described in the opossum by the same author in 1924 "It is that relatively undifferentiated portion of the secondary olfactory area lying between the bulbar formation and the specialized nuclei farther spinalward '

As early as 1912 Rose described the nucleus in various small mammals, among which the guinea pig, as area praepyriformis bulbaris This name he changed later into area retrobulbaris (Rose, 1926) He describes the area, a cortex holoprotoptychos bistratificatus, as a two-layered cortex, consisting of a lamina zonalis and a pyramidal cell layer lying beneath it

The anterior olfactory nucleus, as decribed by Johnston (1923, a) in various mammals and in the white rat by Gurdjian (1925), only comprises the posterior part of the nucleus described by Herrick The lateral and basal parts which lie in front of this are considered by them as belonging to the piriform lobe the medial part as belonging to the nucleus parolfactorius medialis (nucleus medialis septi)

Descriptions of the anterior olfactory nucleus in rodents are given for the mouse by Rose (1929), for the rabbit by Rose (1931) and Young (1936), for the squirrel and the mouse by Crosby and Humphrey (1939, a) and for the guinea pig by Johnson (1957, a) Fox (1940) described the nucleus in the cat

The anterior olfactory nucleus is divisible topographically into a pars lateralis, dorsalis, medialis, ventralis, and caudalis (Rose) or posterior (Crosby and Humphrey, Fox) and a pars externa Rose based the subdivision upon differences in structure, which are said to be particularly conspicious in the rabbit, e g "Die Area retrobulbaris dorsalis enthalt so schon geformte Pyramidenzellen, wie wir es sonst in keiner Area der retrobulbaren Region vorfinden"

Apart from the pars externa, which clearly differs from the rest of the anterior olfactory

nucleus, none of the other authors mentions a clear distinction in cell type and arrangement between the various parts of the nucleus Only in the mouse Crosby and Humphrey (1939, a) mention „The portions are of a similar cell character, but there are differences in arrangement which are particularly marked in the looser spacing of the neurons in the middle part of the pars medialis" Moreover, the neurons of the pars posterior of the mouse are said by them to be bigger and more darkly staining than the cells of the pars medialis

In the guinea pig we were able to indicate certain differences in cell size and cell arrangement between the various portions of the anterior olfactory nucleus

As regards the pars rostralis as described by us, already Cajal (1902) observed that beneath the granular cell layer of the accessory olfactory bulb a conglomeration of large or medium-sized, ovoid or polygonal neurons occurs, well developed in the guinea pig, less in the rabbit and the mouse

In his opinion these cells are possibly displaced Golgi cells, which really belong to the granular cell layer of the accessory bulb Herrick (1924) considered these cells a pars bulbaris of the anterior olfactory nucleus Also in the rabbit (Young, 1936) and the cat (Fox, 1940) cell groups, which are entirely intrabulbary, are present These are however not considered by these authors an apart portion of the anterior olfactory nucleus

In the guinea pig a considerable part of the nucleus olfactorius anterior is actually included within the olfactory bulb Beside a pars rostralis, which is situated entirely intrabulbarly and mostly lies detached from the rest of the anterior nucleus, also the pars lateralis and pars dorsalis have continuations from the peduncle in the olfactory bulb

This extension of the anterior olfactory nucleus in the bulbar area is in our opinion essential for the interpretation of the results of experiments in this field

Caudalward the anterior olfactory nucleus grades over dorsally into the neocortex, laterally into the prepiriform cortex, ventrally into the olfactory tubercle and nucleus accumbens, and medially into the septal area and the anterior or precommissural part of the hippocampus That these transitions are not always sharp, is already pointed out by Herrick (1924) "My own practice is to extend the nucleus olfactorius anterior as far backward as the tissue is structurally undifferentiated, and where obvious histological change occur to give the tissue its customary designation, as tuberculum olfactorium, etc "

In the guinea pig this applies especially to the transition from the anterior olfactory nucleus to the prepiriform cortex and the olfactory tubercle The transition from the pars dorsalis into the neocortex is a distinct one whereas the pars posterior is separated from the nucleus accumbens by a plexiform layer The transition from the pars medialis into the precommissural hippocampus takes place at the level of the rostral tip of the tuberculum olfactorium This implies, in contrast with data of other authors, that the precommissural hippocampus of the guinea pig is hardly extending into the olfactory peduncle (fig 4)

Herrick (1924) describes that the formatio hippocampi in the opossum extends rostrally as far as the olfactory bulb The superficial cell layer of the pars medialis of the anterior olfactory nucleus is called by him cortex hippocampi anterior or cortex hippocampi cruralis "At the dorsomedial angle of the crus there is a superficial lamella of cells which is the rostral end of the hippocampal formation"

Rose (1912 1926) indicates that in most of the animals studied by him the extension in the olfactory peduncle of the precommissural hippocampus (taenia tecta) reaches as far as the area praepyriformis bulbaris (area retrobulbaris) For particulars the reader is referred to the original publications

In the rabbit (Young 1936) the precommissural hippocampus begins near the base of the olfactory peduncle in the medial part of the anterior olfactory nucleus as a group of moderately large oval and rounded cells among which are scattered a few intensely stained neurons At the level of the rostral extreme of the nucleus caudatus it appears as a group of deeply stained cells in the ventromedial angle of the hemisphere

According to Crosby and Humphrey (1939 a) the precommissural hippocampus in the mouse is relatively very large and easily to be distinguished from the pars medialis The cell group is situated in the ventromedial angle of the olfactory peduncle where it forms an eminence on the ventral surface of the brain It extends forward in the peduncle to a level just rostral to the transition from the pars dorsalis into the frontal neocortex

Cortex praepiriformis

The prepiriform cortex (figs 12-20 27-30) or gyrus olfactorius lateralis (ecorce du lobe frontale sous-jacente a la racine externe of Cajal 1911) is situated in the anterobasal part of the hemisphere

It is bounded laterally by the neocortex and separated from this by the fissura rhinalis In its anterior part it is bounded medially by the nucleus olfactorius anterior pars ventralis in its posterior part by the tuberculum olfactorium

A fissura rhinalis arcuata (fissura endorhinalis) is only present between the prepiriform cortex and the posterior part of the olfactory tubercle (fig 18)

Rostrally the prepiriform cortex blends very gradually into the pars lateralis of the anterior olfactory nucleus caudally the transition into the periamygdaloid cortex is indicated by the incisura olfactoria (Gastaut and Jammers 1961)

A such-like subdivision of the prepiriform cortex as given by Calleja (1893), Cajal (1911) and O Leary (1937) applies to the guinea pig

1 Fibrillar layer This layer consists of the fibres and collaterals of the lateral olfactory tract

2 Plexiform or molecular layer

3 Layer of small and medium-sized pyramidal cells or layer of superficial polymorph cells (Cajal) In this compact cell layer are mostly found medium-sized neurons (fig 45 D 2)

4 Polymorph layer which contains few neurons These are large cells some of which are even larger than the cells of the pyramidal cell layer

Calleja and O Leary subdivide this layer again into 4a) layer of large pyramidal cells and 4b) layer of polymorph cells Notable in this layer are the large neurons which are present near the spot where the anterior limb of the anterior commissure turns medialward (fig 30)

Rose (1931) and Mittelstrass (1937) distinguish in the prepiriform cortex a lateral and a medial part the regio praepyriformis lateralis (Prpy1) and regio praepyriformis medialis (Prpy2) According to Rose the regio praepyriformis medialis is a cortex semiparietinus and

comprises three layers a lamina zonalis, a wide cell layer and a polymorph layer The lateral prepiriform region is a cortex palliostriatalis by virtue of its way of development and the presence of a claustrum

However, in the guinea pig we are under the impression that this latter cortex may better be considered as a transitional zone between the prepiriform cortex ventrally and the area agranularis ventralis and posterior dorsally

Area olfactoria

Tuberculum olfactorium

The olfactory tubercle (figs 14-19, 31, 32), or lobus parolfactorius of Beccari (1910) and Edinger (1911), is in the guinea pig a slightly prominent structure on the ventral side of the hemisphere It has a triangular shape, the apex lying rostrally and the base caudally

The tubercle lies between the ventral part of the anterior olfactory nucleus rostrally, the prepiriform cortex laterally, the medial septal nucleus medially and the diagonal band of Broca medially and caudally A fissura rhinalis arcuata which indicates the boundary with the prepiriform cortex, is in the almost completely lissencephalic brain of the guinea pig only present in the posterior part of the olfactory tubercle (fig 18) By way of this fissure the lateral striate arteries reach the striatum (Johnston, 1923 a) On the dorsal side the nucleus accumbens is situated

The deepest layer of the tubercle is rostrally separated from this nucleus by a plexiform layer Caudally a strio-tubercular fusion takes place (Obenchain, 1925)

The olfactory tubercle consists of three layers

1 Plexiform layer

2 Pyramidal cell layer This layer consists of small and medium-sized neurons (fig 45, D 3) together with a few granular cells

3 Polymorph cell layer In this lamina are found predominantly medium-sized neurons and also some large neurons of the efferent type, such as described in the rat by Gurdjian (1925), in the rabbit by Young (1936) and in the cat by Fox (1940) The two inner cell layers, however, are only clearly distinguishable from one another in the posterior part of the tubercle Moreover, the pyramidal cell layer is corrugated laterally here

According to Cajal the area perforata anterior in man and the tuberculum olfactorium in mammals may be subdivided into lateral, intermediate and medial portions Such a subdivision is also demonstrated by Young (1936) in the rabbit, by Johnson (1957 a) in the guinea pig and by Fox (1940) in the cat

Pronounced differences between these portions of the olfactory tubercle of the guinea pig could not be established by us It must be noted, however, that in the lateral part of the tubercle and mainly in the anterolateral part compact dish-shaped conglomerations of small neurons occur These cell accumulations are lying in the deep part of the plexiform layer on the border-line of this layer and the pyramidal cell layer That is the reason why this part of the olfactory tubercle bears more resemblance in structure to the prepiriform cortex than to the rest of the tubercle (fig 3)

Fig. 3. Photomicrograph of frontal section at the level of the anterior part of the tuberculum olfactorium, showing the transition from the prepiriform cortex (to the left) to the tuberculum olfactorium (to the right). Klüver-Barrera method. Magnification 45X

The cells of these cell groups (fig. 46, A 1), however, are much smaller than those of the pyramidal cell layer of the prepiriform cortex (fig. 45, D 2). They have the same size as the cells of the pars externa of the anterior olfactory nucleus. Beside these accumulations of small neurons there also occur many islands of granular cells, and this predominantly in the plexiform layer. Just as a.o. in the oppossum and the cat, a large granular island is also present in the guinea pig medially between the nucleus accumbens and the lateral septal nucleus (fig. 18, 29-31).

The third type of the islands of Calleja as mentioned by Loo (1931), islands of medium-sized pyramidal cells, are very scarce in the olfactory tubercle of the guinea pig.

Substantia perforata anterior

An area perforata anterior, as described in Orycteropus by Sonntag and Woollard (1925), is not present in the guinea pig. Most of the blood vessels, which provide the striatum, enter the brain via the fissura rhinalis arcuata.

Gyrus diagonalis

The nucleus of the diagonal band of Broca (figs. 18-22, 27-32) is continuous rostrally with the nucleus medialis septi. Just as this one the left and right nuclei of Broca join in the midline. Caudal to the olfactory tubercle the nucleus extends ventrolateralward as far as the

prepiriform cortex In our sections of the guinea pig we could not clearly distinguish a ventral and a dorsal stream of cells in this fanning-out, as decribed by Young (1936), Fox (1940) and Johnson (1957 a)

The nucleus of the diagonal band is notable on account of its very large cells (fig 46, A 2), apart from its richness in fibres

Area septalis

Under the name „area septalis" or „septum" we understand the area that lies beneath the corpus callosum in the anteromedial wall of the hemisphere

Rostrally it extends as far as the frontal cortex and the anterior olfactory nucleus, caudally as far as the hippocampal commissure and laterally as far as the lateral ventricle On the ventral side it is bounded rostrally by the olfactory tubercle and caudally by the area preoptica

A portion of the septal area is rostral to the anterior commissure, the precommissural septum As recorded by Hines (1929) this part of the septum was named by Elliot Smith successively area praecommissuralis (1896), corpus praecommissurale (1897), corpus paracommissurale (1899) and finally corpus paraterminale (1903) Another name for this area is gyrus subcallosus (Elliot Smith, 1937, Craigie, 1925)

The postcommissural septum, also called pars supraforaminalis or pars fimbrialis septi (Craigie, 1925), may be considered identical with the septum pellucidum in man

The area septalis is subdivided by Johnston (1913) into the area parolfactoria and the primordium hippocampi This subdivision, however, does not agree with our classification into pre- and postcommissural septum (see Johnston, 1913, fig 89)

The nuclei of the area septalis of the guinea pig may be subdivided into medial and lateral nuclei

Medial nuclei

Precommissural part of the hippocampus (nucleus hippocampi anterior or taenia tecta) This portion of the hippocampus (figs 4, 15, 16, 28), lying between the frontal cortex and the medial septal nucleus, is really part of the lobus limbicus and not of the olfactory lobe (Gastaut and Lammers, 1961)

Dorsocaudally the nucleus is continuous with the induseum griseum and ventrally with the pars medialis of the anterior olfactory nucleus Right beneath the genu of the corpus callosum it bends slightly caudalward

The taenia tecta, which in the guinea pig consists of medium-sized cells (fig 46, A 3) with darkly staining Nissl substance, is described by Rose (1926) as a cortex holoprotoptychos bistratificatus

Nucleus septohippocampalis (figs 4, 17, 18, 27) The nucleus septohippocampalis may be regarded as a caudal extension of the precommissural hippocampus right beneath the corpus callosum The existence and extent of the nucleus in mammals is very differently stated by various authors Thus Craigie (1925) reports that the nucleus is present in the albino rat, whereas in the same animal it could not be clearly distinguished from the other septal nuclei

by Sanders-Woudstra (1961). According to Young (1936) the nucleus is distinctly present in the rabbit and extends dorsally as far as the bed nucleus of the commissura fornicis. By Fox (1940) the nucleus could only be identified in very young kittens, and also in these animals it was not always present bilaterally.

In contrast with Johnson (1957 a) we could always indicate the nucleus septohippocampalis of the guinea pig very clearly, in frontal as well as in sagittal and horizontal sections. In this animal the nucleus is only found beneath the genu of the corpus callosum and it contains larger cells (fig. 46, B 1) than the anterior hippocampal nucleus.

The nucleus dorsalis septi in the opossum, described by Loo (1931), lies in the same position as the nucleus septohippocampalis of the guinea pig.

Nucleus medialis septi (figs. 4, 15-22, 26-29). This nucleus makes its appearance rostrally between the precommissural hippocampus and the tuberculum olfactorium. More caudalward the nucleus extends dorsally and reaches the corpus callosum caudal to the nucleus septohippocampalis. Dorsal to the fornix the medial septal nucleus passes on into the postcommissural part of the septal area (fig. 4).

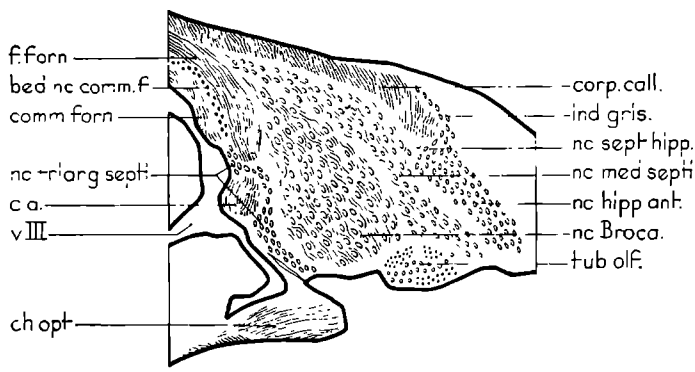


Fig. 4. Drawing of a sagittal section through the area septalis of an adult guinea pig. Series 378-760. Kluver-Barrera method. 10 μ. Magnification 10 ×. The level of the section is indicated in fig. 5, b. A list of abbreviations is given on p 28,29.

The left and right nuclei join in the midline. The cells of the medial septal nucleus are medium-sized (fig. 46, B 2) and contain darkly staining Nissl substance. Owing to its great richness in fibres running vertically, the nucleus is very clearly defined.

In the guinea pig, as in the bat, it is not possible to divide the medial septal nucleus into an anterior small-celled and a posterior large-celled portion, such as is reported in the opossum (Loo, 1931) and in the cat (Fox, 1940) or into an anterior large-celled and a posterior small-celled portion such as Young (1936) describes in the rabbit.

The caudal surface of the medial septal nucleus is concave and is continuous with the nucleus of the diagonal band of Broca (fig. 4).

Bed nucleus of the commissura fornicis (bed nucleus of the commissura hippocampi ven-

nalis) This nucleus (figs 4, 23, 26, 27), which is called by Andy and Stephan (1959, 1962) nucleus triangularis septi, consists of small neurons (fig 46, B 3), very closely packed, which chiefly lie between both fornices and the commissura fornicis, and to a less extent among the commissural fibres

Nucleus triangularis septi (figs 4, 22, 28-31) In a frontal section (fig 22) the triangular septal nucleus is found in the triangular space between both columnae fornicis and the anterior commissure It consists chiefly of cells (fig 46, C 1), which are a little smaller than the cells of the nucleus septalis fimbrialis and larger than those of the bed nucleus of the commissura fornicis In its rostral part are also found a few large neurons, which indicate the coherence of the nucleus with the nucleus of the diagonal band of Broca, which lies immediately rostral to it Caudally the nucleus is continuous with the bed nucleus of the commissura fornicis on both sides of the midline

In a sagittal section (fig 4) one may clearly see the triangular nucleus extending in the midline as a narrow stream of cells, rostral of the anterior commissure and the third ventricle, as far downwards as the bottom of the precommissural septum This is also decribed in the mink by Jeserich (1945)

There is confusion in the literature as to the position of the triangular nucleus in the septal area From the original description of Cajal (1955) "We call the triangular nucleus that medial grey mass situated in the triangle formed posteriorly by the ventral psalterium and rostrally and on both sides by the superior (almost horizontal) portion of the anterior pillars", it clearly follows that this nucleus is situated in the, at a horizontal section triangular space which is bordered caudally by the commissura fornicis and anterolaterally by both fimbriae fornicis Thus the triangular nucleus of Cajal may be identified with the bed nucleus of the commissura fornicis or a condensation of it, as is described by Loo (1931), Young (1936) and Fox (1940)

The triangular septal nucleus, as described by us in the guinea pig, which lies between both columnae fornicis and the anterior commissure and which, as far as cell structure is concerned, clearly differs from the bed nucleus of the commissura fornicis, is called nucleus supracommissuralis by Bosque et al (1959) and nucleus preopticus medianus by Humphrey and by Andy and Stephan (1959, 1962)

It is of interest to note that the nucleus preopticus medianus, described by Loo (1931) in the opossum is situated beneath the anterior commissure, separated from this by a medial extension of the nucleus preopticus anterior The nucleus preopticus medianus, described by Bauchot (1959) in Talpa europaea, is also situated beneath the anterior commissure

Bed nucleus of the anterior commissure (figs 21, 29-31) The cells of this nucleus (fig 46, C 2), which according to Johnston (1923 a) have migrated from the lateral olfactory area, are lying not only among the fibres of the anterior commissure but are mainly situated on its rostral side between the nucleus of Broca and the commissure

Lateral nuclei

Nucleus lateralis septi (figs 17-23, 25-28) The lateral septal nucleus makes its appearance a little more caudally than the medial septal nucleus and may be considered as a dorsolateral

extension of this nucleus There does not exist a clear-cut line of demarcation between the two nuclei, but the cells of the lateral nucleus (fig 46, C 3) are a little smaller than those of the medial one Moreover, the lateral nucleus contains less fibres

Rostrally (figs 17, 18) the lateral septal nucleus may be clearly distinguished from the nucleus accumbens The latter nucleus has small neurons (fig 46, D 1) with little Nissl substance and contains few or no myelinated fibres Between both nuclei a cell-free zona limitans is present, just as in the rabbit (Young, 1936) Caudalward the lateral septal nucleus increases very much in size, while the number of fibres diminishes and the boundary with the nucleus accumbens becomes indistinct

When the nucleus septalis fimbrialis makes its appearance the lateral septal nucleus becomes smaller again and becomes situated in the periphery of the septal area

In the macacus and panda (Lauer, 1945, 1949), in the mink (Jeserich, 1945) and in Galago demidovii and Soricidae (Andy and Stephan, 1959, 1962) the lateral septal nucleus can be divided along its whole frontocaudal extent into a dorsal group (nucleus septalis dorsalis of Andy and Stephan) and a ventral group (nucleus septalis lateralis of Andy and Stephan) In the opossum (Loo, 1931) this division is only possible at the level of the anterior commissure

In the guinea pig, as in the bat and the cat, such a division of the lateral septal nucleus cannot be made However, at the level of the anterior commissure the cells in the ventral part of the nucleus are more compactly arranged and are slightly smaller than the cells in the dorsal part

At the level of the caudal tip of the olfactory tubercle (fig 19) a modest oval group of cells, notable by its lack of fibres, is present between the lateral septal nucleus and the dorsal extremity of the nucleus of Broca

Its cells exhibit the same aspect as the cells of the lateral septal nucleus Only by Lauer (1945) in the macacus a such-like cell group is reported

Nucleus septalis fimbrialis (figs 22, 23, 25-27) This nucleus is present in the postcommissural septum The large cells of the nucleus (fig 46, D 2) lie scattered among the fibres of the fimbria fornicis

Abbreviations

a amygd ant	area amygdaloidea anterior
alv	alveus
a preopt	area preoptica
a sept	area septalis
bed nc c a	bed nucleus of the commissura anterior
bed nc comm forn	bed nucleus of the commissura fornicis
bulb olf str glom	bulbus olfactorius stratum glomerulare
bulb olf str mitr	bulbus olfactorius stratum mitrale
bulb olf acc str glom	bulbus olfactorius accessorius stratum glomerulare
bulb olf acc str mitr	bulbus olfactorius accessorius stratum mitrale
c a	commissura anterior
c a p olf	commissura anterior pars olfactoria
c a p post	commissura anterior pars posterior
caps	capsula
caps ext	capsula externa
caps int	capsula interna
ch opt	chiasma opticum
cl	claustrum
col forn	columna fornicis
comm forn	commissura fornicis
corp amygd	corpus amygdaloideum
corp call	corpus callosum
corp call f a	corpus callosum forceps anterior
cort amygd tr a	cortico-amygdaloid transition area
cort periamygd	cortex periamygdaloidea
cort praepir	cortex praepiriformis
f forn	fimbria fornicis
f rhin	fissura rhinalis
f rhin arc	fissura rhinalis arcuata
f rhin med	fissura rhinalis medialis

hipp	hippocampus
ind gris	indusium griseum
isl gran	island of granular cells
isl gran med	large medial island of granular cells
isl sm neur	island of small neurons
m f b	medial forebrain bundle
m interc	massa intercalata
nc acc	nucleus accumbens
nc bas amygd	nucleus basalis amygdalae
nc Broca	nucleus of Broca
nc caud	nucleus caudatus
nc cort amygd	nucleus corticalis amygdalae
nc hipp ant	nucleus hippocampi anterior
nc lat amygd	nucleus lateralis amygdalae
nc lat septi	nucleus lateralis septi
nc med amygd	nucleus medialis amygdalae
nc med septi	nucleus medialis septi
nc olf ant p ext	nucleus olfactorius anterior, pars dorsalis
nc olf ant p dors	nucleus olfactorius anterior pars externa
nc olf ant p lat	nucleus olfactorius anterior pars lateralis
nc olf ant p med.	nucleus olfactorius anterior pars medialis
nc olf ant p post	nucleus olfactorius anterior, pars posterior
nc olf ant p rostr	nucleus olfactorius anterior pars rostralis
nc olf. ant p ventr	nucleus olfactorius anterior, pars ventralis
nc sept fimbr	nucleus septalis fimbrialis
nc sept hipp	nucleus septohippocampalis
nc supracot	nucleus supraopticus
nc triang septi	nucleus triangularis septi
nc tr olf lat	nucleus of the tractus olfactorius lateralis
n opt	nervus opticus
ped cer	pedunculus cerebri
put	putamen
tr olf lat	tractus olfactorius lateralis
tr opt	tractus opticus
tub olf	tuberculum olfactorium
tub olf l polym	tuberculum olfactorium lamina polymorphia
tub olf l pyr	tuberculum olfactorium lamina pyramidalis
v lat	ventriculus lateralis
v olf	ventriculus olfactorius
v III	ventriculus tertius

Fig. 5. Brain of an adult guinea pig. a) lateral view, b) ventral view, c) dorsal view. In fig. 5, a are indicated the levels of the figures 24, 29 and 34; in fig. 5, b the levels of the figures 4, 6, 14 and 22.

Fig 5a

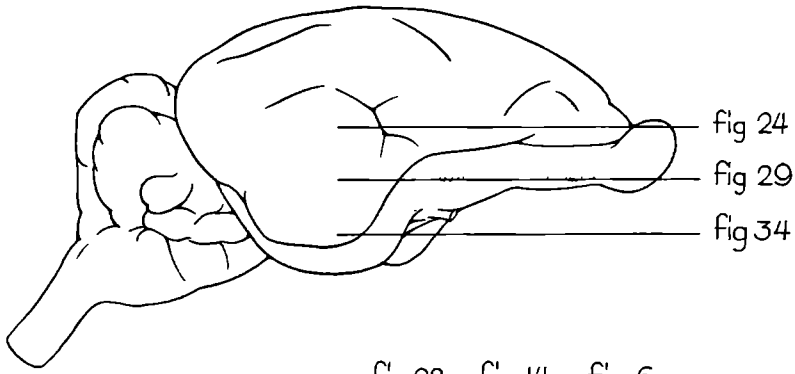


fig 22 fig 14 fig 6

Fig 5b

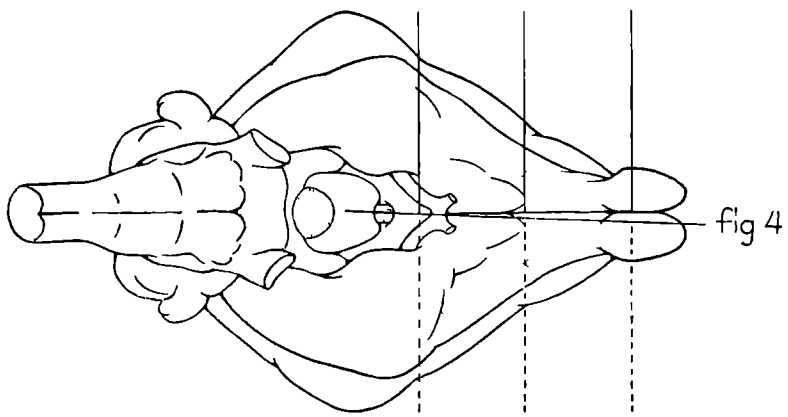
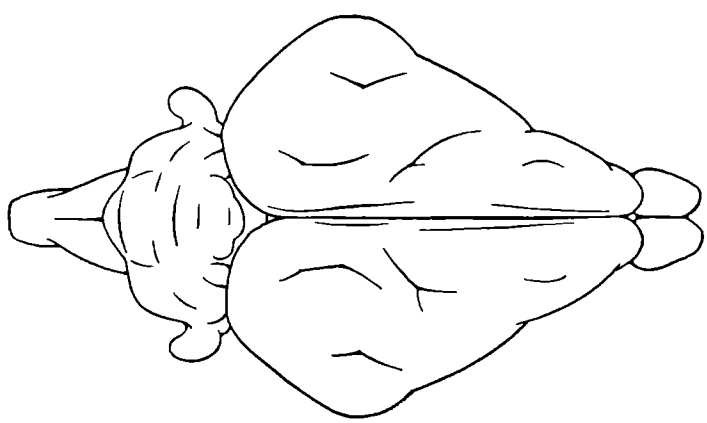


Fig 5c



Figs 6–23 Drawings of serial frontal sections through the anterior olfactory lobe of an 11 days old guinea pig
Series 334 Kluver-Barrera method 15 μ Magnification 14 $\times$
The interval between two successive sections is 375 μ
The levels of the figures 6 14 and 22 are indicated in fig 5, b

Fig 6 Frontal section through the rostral extreme of the accessory olfactory bulb showing the pars rostralis of the anterior olfactory nucleus

Fig 7 Frontal section through the middle third of the accessory olfactory bulb

Fig 8 Frontal section through the posterior third of the accessory olfactory bulb showing the rostral extremes of the lateral dorsal and external parts of the anterior olfactory nucleus

Fig 9 Frontal section through the olfactory peduncle slightly rostral to the pars medialis of the anterior olfactory nucleus

Fig 6

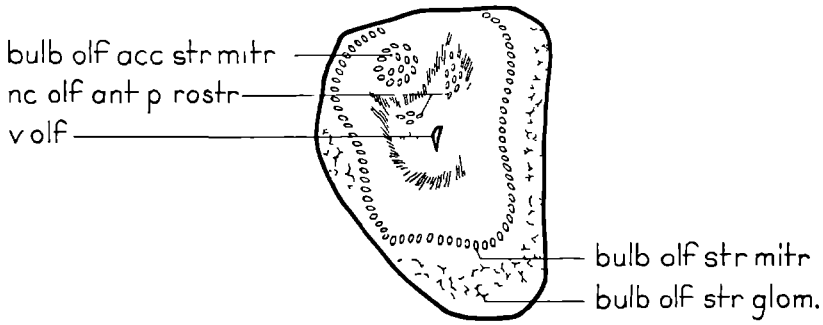


Fig 7

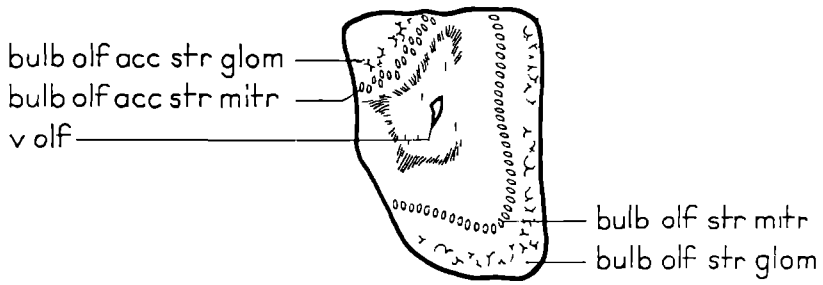


Fig 8

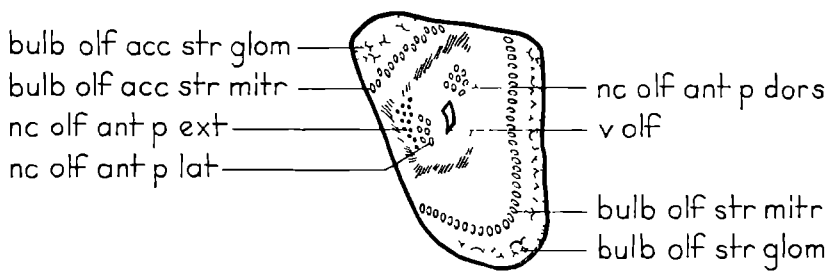


Fig 9

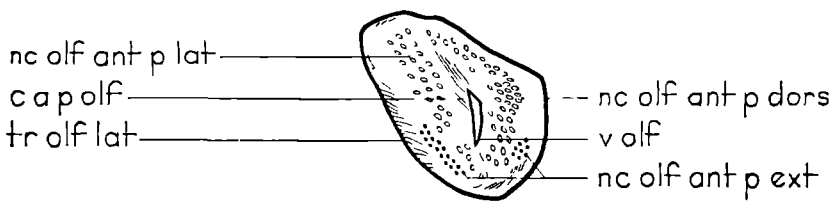


Fig. 10. Frontal section through the olfactory peduncle at the level of the rostral end of the pars medialis of the anterior olfactory nucleus.

Fig 11. Frontal section through the middle of the olfactory peduncle.

Fig 12. Frontal section through the posterior third of the olfactory peduncle, showing the rostral extreme of the prepiriform cortex and the pars posterior of the nucleus olfactorius anterior.

Fig. 13. Frontal section through the posterior part of the olfactory peduncle slightly rostral to the tuberculum olfactorium.

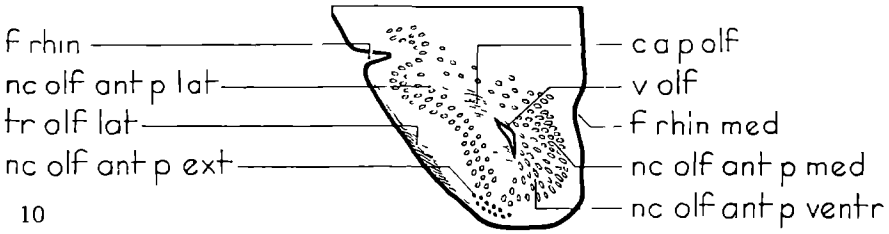


Fig 10

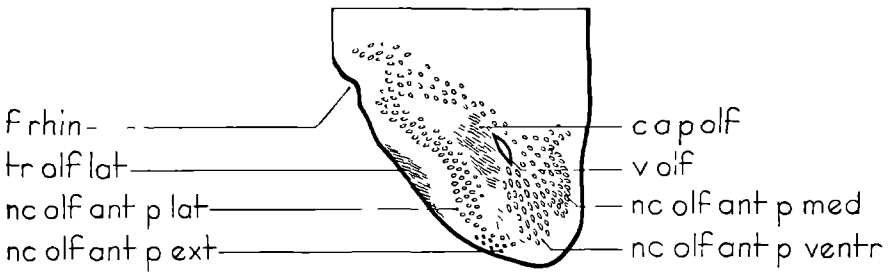


Fig 11

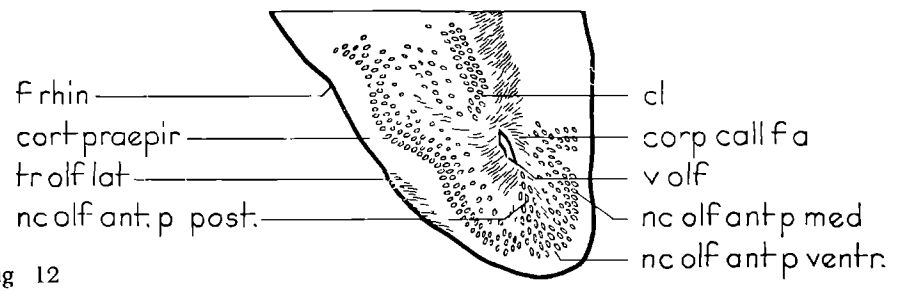


Fig 12

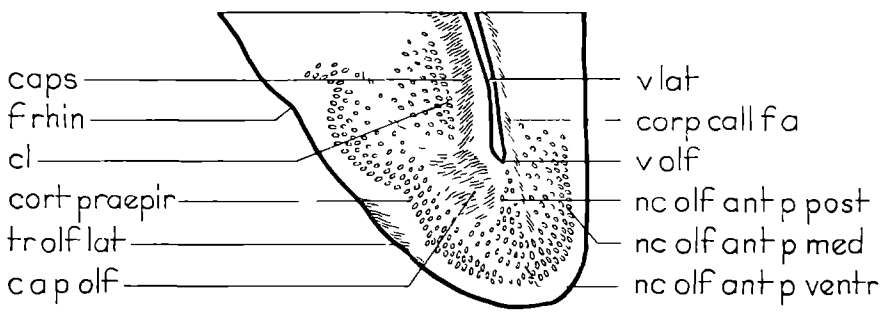


Fig 13

Fig 14 Frontal section at the level of the rostral extreme of the tuberculum olfactorium

Fig 15 Frontal section through the anterior third of the tuberculum olfactorium, showing the anterior end of the nucleus hippocampi anterior and the nucleus medialis septi

Fig 16 Frontal section through the middle of the tuberculum olfactorium

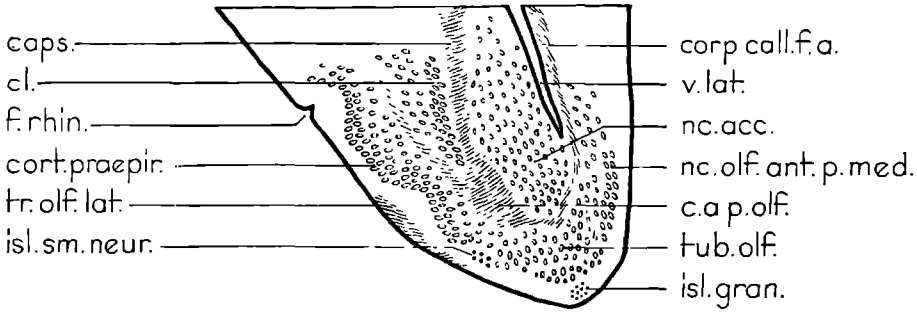


Fig. 14

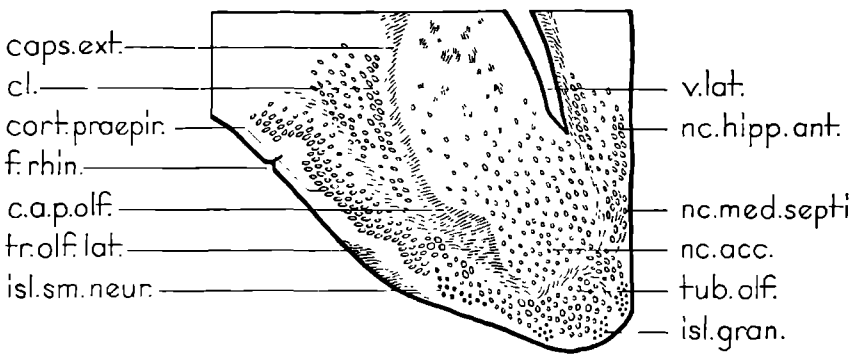


Fig. 15

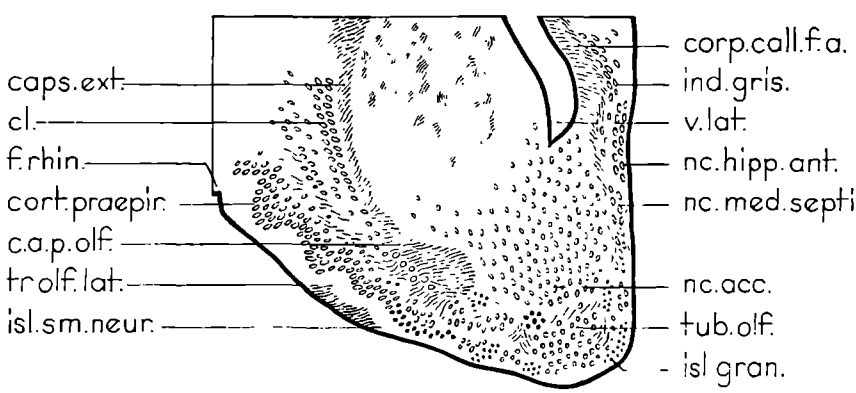


Fig. 16

Fig. 17. Frontal section through the posterior part of the tuberculum olfactorium and the rostral extreme of the lateral septal nucleus

Fig 18. Frontal section through the posterior part of the tuberculum olfactorium, cutting the large medial island of granular cells

Fig. 19 Frontal section through the caudal extreme of the tuberculum olfactorium.

Fig. 17

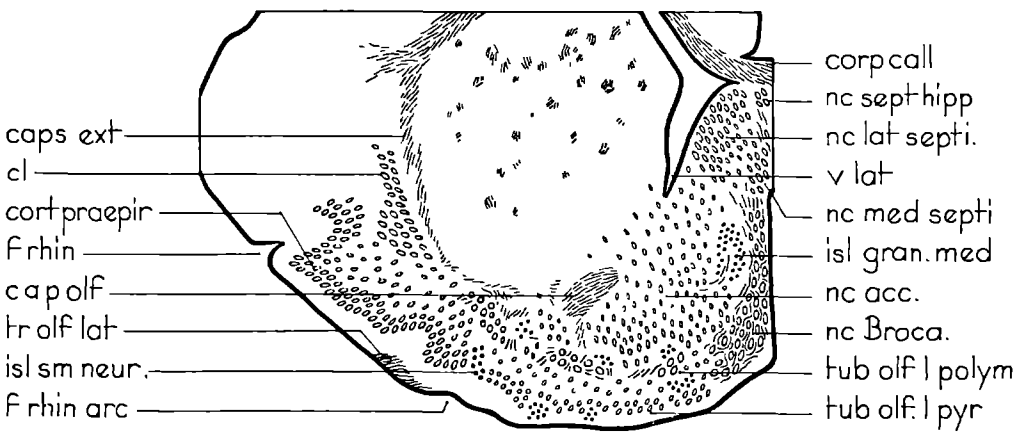


Fig. 18

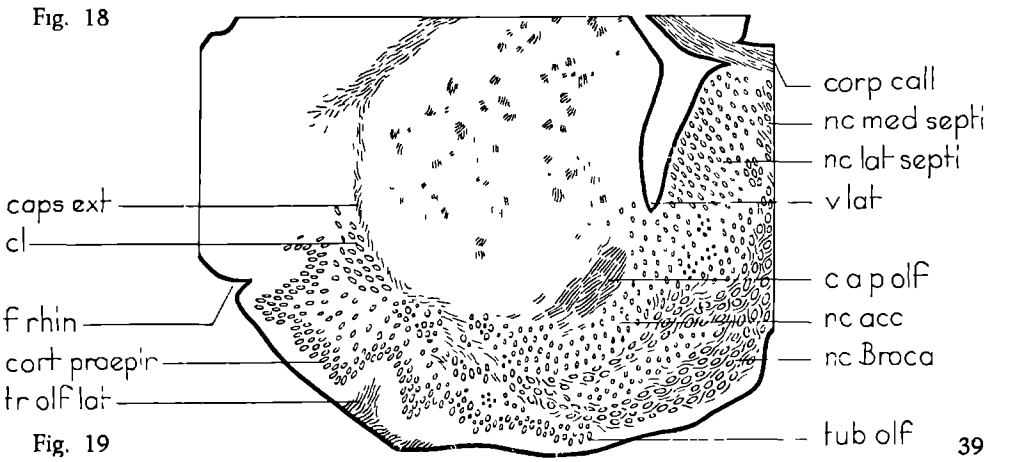
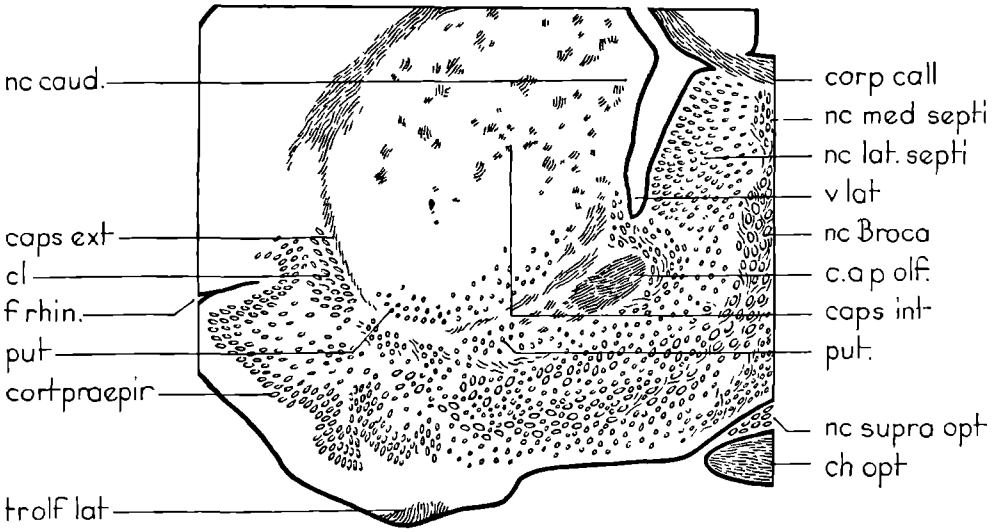


Fig. 19

Fig 20 Frontal section through the caudal end of the prepiriform cortex slightly rostral to the incisura olfactoria.

Fig 21. Frontal section through the anterior amygdaloid area.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f rhin.
put
cort praepir
tr olf lat
corp call
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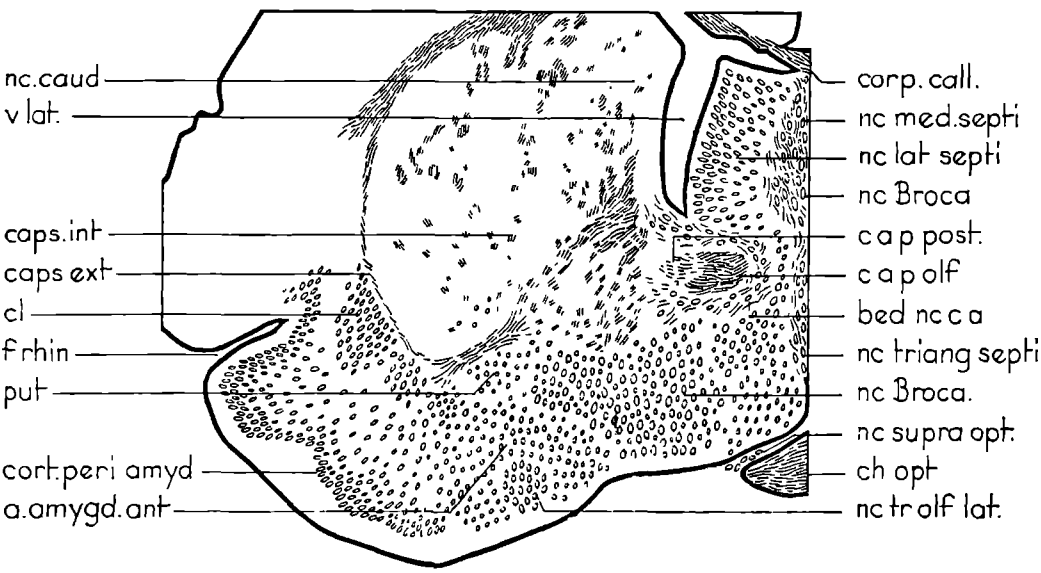
caps int
put.
nc supra opt
ch opt

Fig. 20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nc Broca
c a p post.
c a p olf
bed nc c a
nc triang septi
nc Broca.
nc supra opt.
ch opt
nc tr olf lat.

Fig. 21

Fig. 22. Frontal section through the anterior amygdaloid area at the level of the anterior commissure.

Fig. 23. Frontal section at the level of the postcommissural septum.

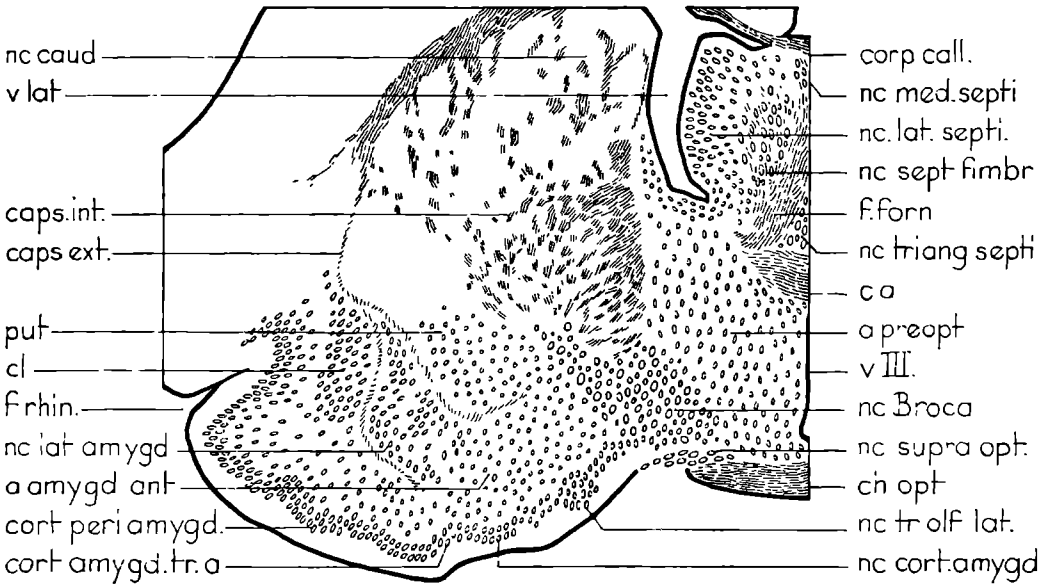

nc caud
v lat
caps.int.
caps ext.
put
cl
f rhin.
nc lat amygd
a amygd ant
cort peri amygd.
cort amygd.tr.a
corp call.
nc med.septi
nc. lat. septi.
nc sept fimbr
f.forn
nc triang septi
c a
a preopt
v III.
nc Broca
nc supra opt.
ch opt
nc tr olf lat.
nc cort.amygd

Fig. 22

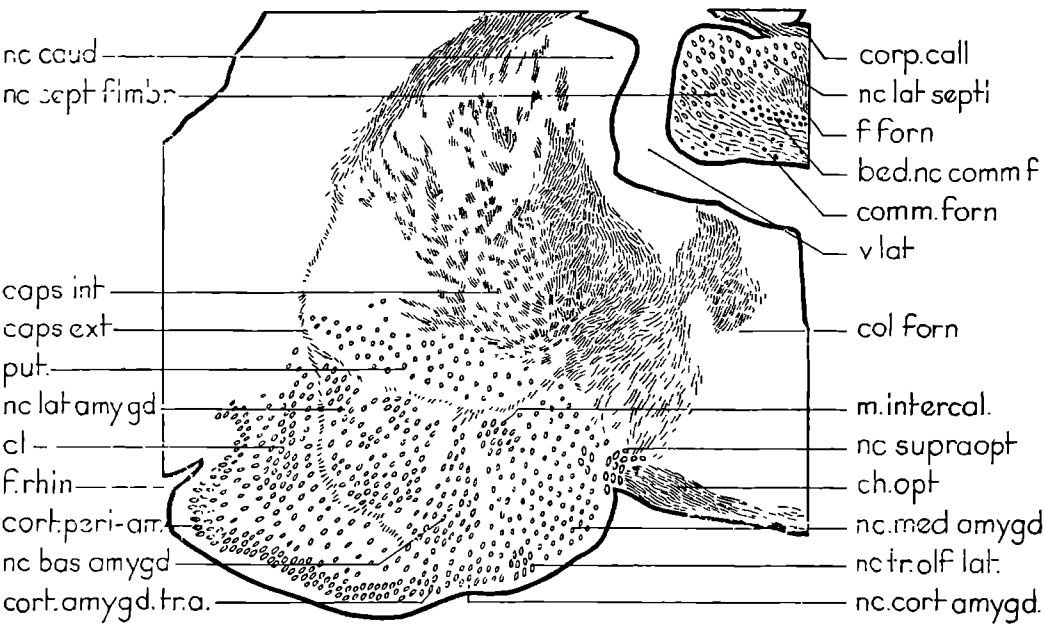

nc caud
nc sept fimbr
caps int
caps ext
put.
nc lat amygd
cl
f.rhin
cort.peri-am.
nc bas amygd
cort.amygd.tr.a.
corp.call
nc lat septi
f forn
bed.nc comm f
comm.forn
v lat
col forn
m.intercal.
nc supraopt
ch.opt
nc.med amygd.
nc tr.olf lat.
nc.cort amygd.

Fig. 23

Figs 24-34 Drawings of serial horizontal sections through the anterior olfactory lobe of an 24 days old guinea pig
Series 354 Kluver-Barrera 10 μ Magnification 14 $\times$
The interval between two successive sections is 500 μ
The levels of the figures 24, 29 and 34 are indicated in fig 5 a

Fig 24 Horizontal section at the level of the dorsal extreme of the olfactory bulb

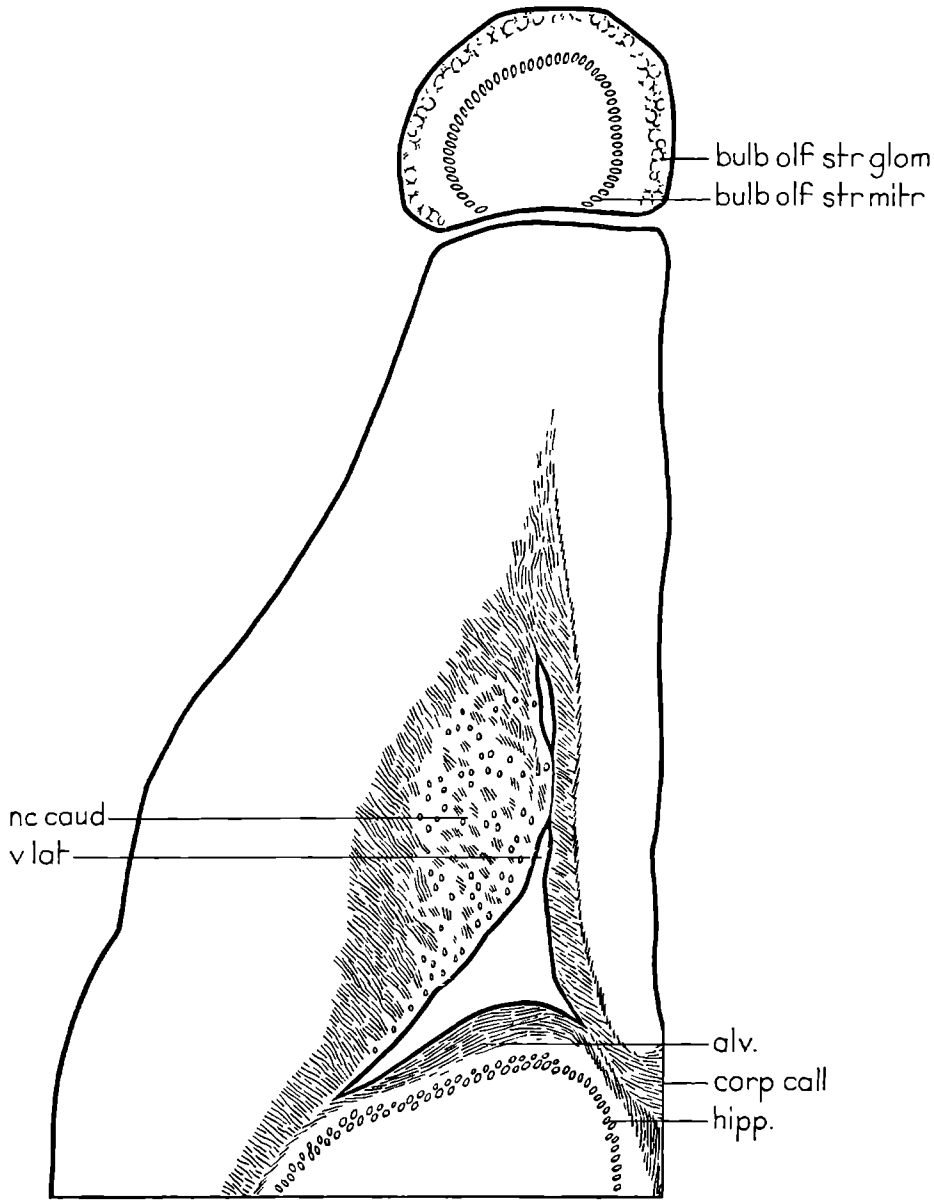

bulb olf str glom
bulb olf str mitr
nc caud
v lat
alv.
corp call
hipp.

Fig. 24

Fig. 25. Horizontal section at the level of the pars rostralis of the anterior olfactory nucleus.

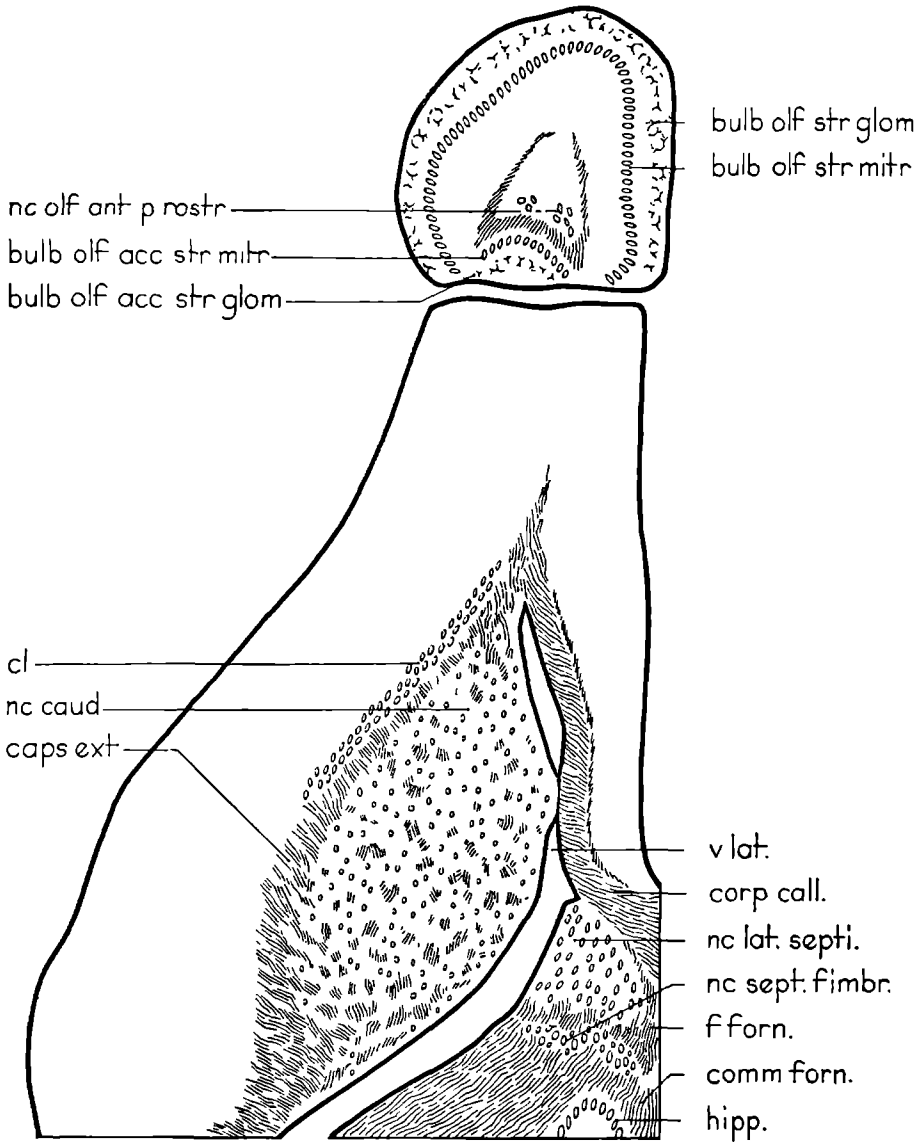

bulb olf str glom
bulb olf str mitr
nc olf ant p rostr
bulb olf acc str mitr
bulb olf acc str glom
cl
nc caud
caps ext
v lat.
corp call.
nc lat. septi.
nc sept. fimbr.
f forn.
comm forn.
hipp.

Fig. 25

Fig. 26 Horizontal section at the level of the ventral third of the accessory olfactory bulb

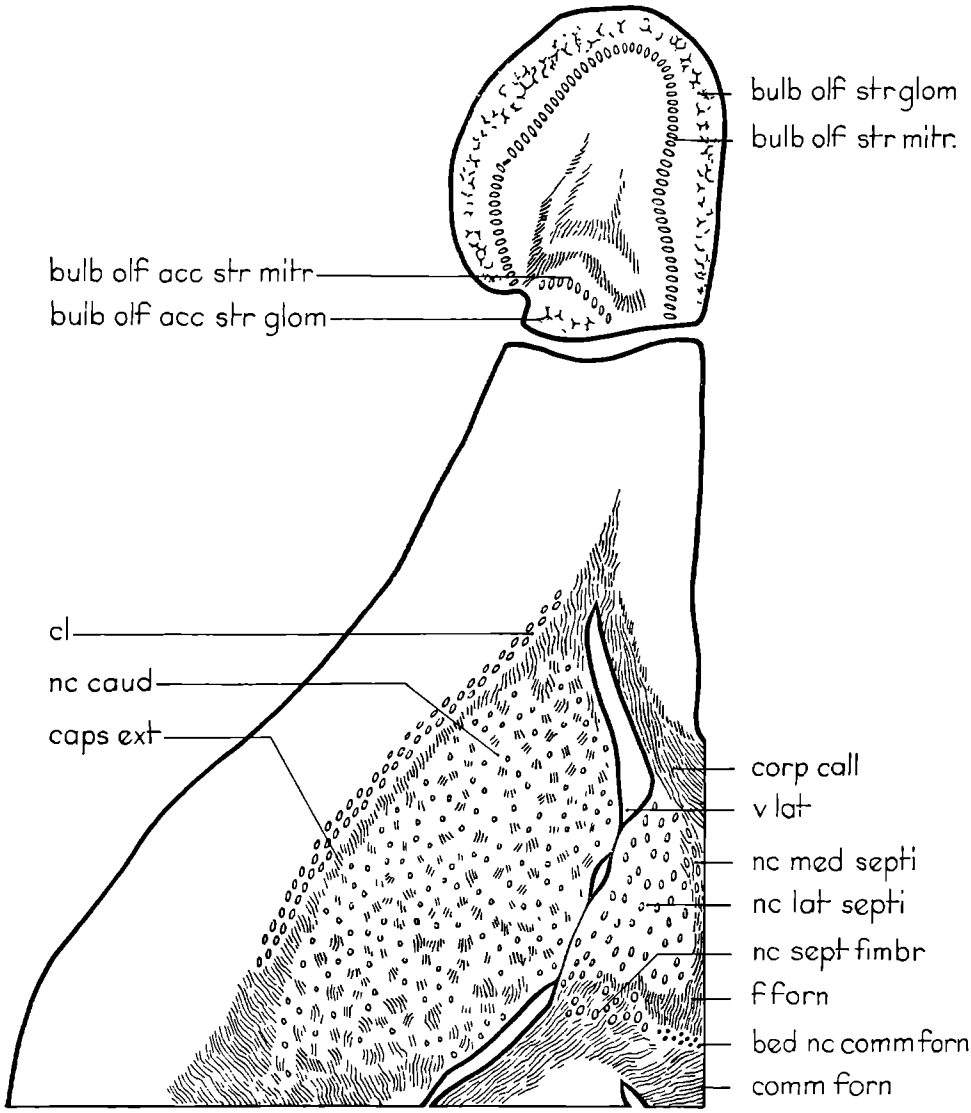

bulb olf str glom
bulb olf str mitr
bulb olf acc str mitr
bulb olf acc str glom
cl
nc caud
caps ext
corp call
v lat
nc med septi
nc lat septi
nc sept fimbr
f forn
bed nc comm forn
comm forn

Fig. 26

Fig 27 Horizontal section at the level of the pars dorsalis of the anterior olfactory nucleus

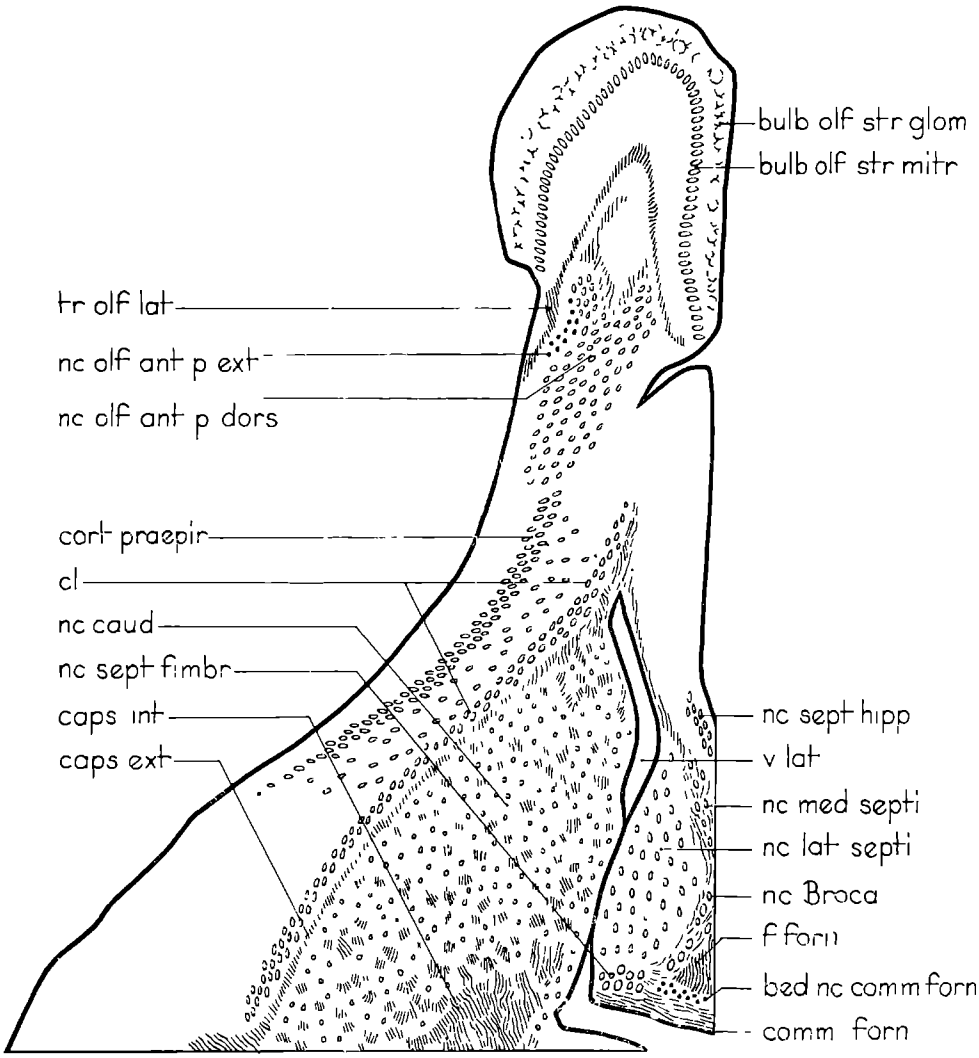

bulb olf str glom
bulb olf str mitr
tr olf lat
nc olf ant p ext
nc olf ant p dors
cort praepir
cl
nc caud
nc sept fimbr
caps int
caps ext
nc sept hipp
v lat
nc med septi
nc lat septi
nc Broca
f forn
bed nc comm forn.
comm forn

Fig 27

Fig 28 Horizontal section at a level slightly dorsal to the pars posterior of the nucleus olfactorius anterior

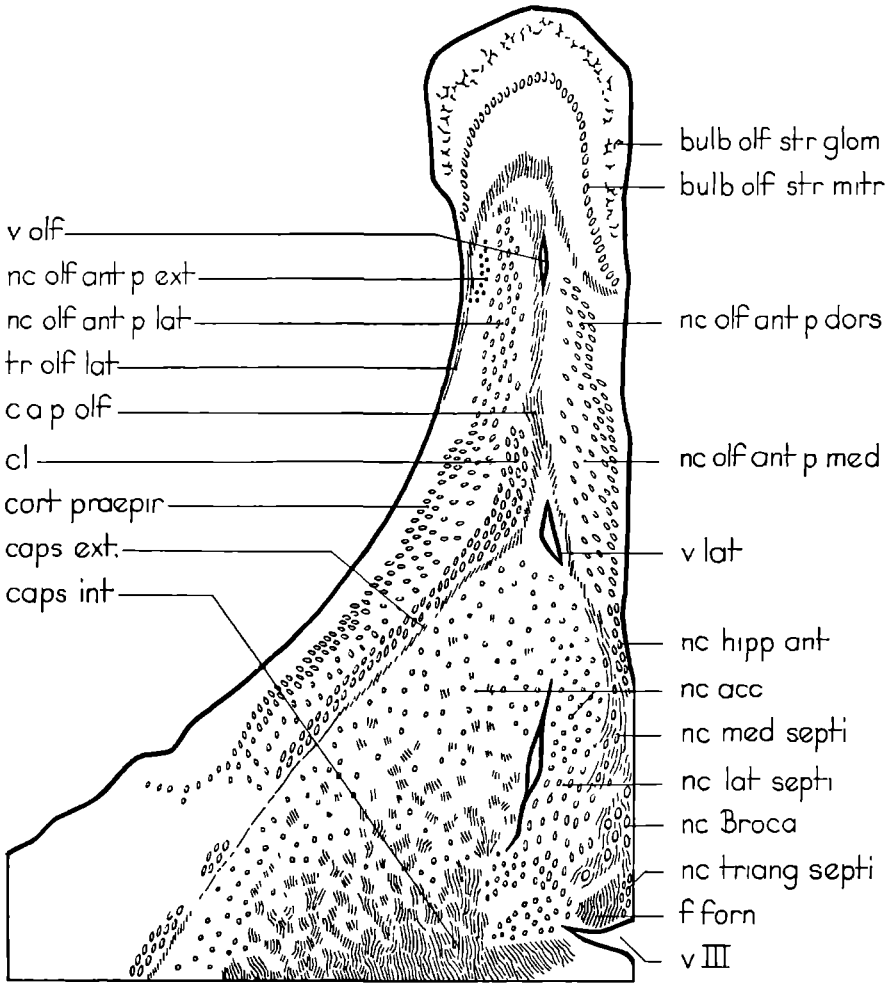

bulb olf str glom
bulb olf str mitr
v olf
nc olf ant p ext
nc olf ant p lat
nc olf ant p dors
tr olf lat
c a p olf
cl
nc olf ant p med
cort praepir
v lat
caps ext.
caps int
nc hipp ant
nc acc
nc med septi
nc lat septi
nc Broca
nc triang septi
f forn
v III

Fig. 28

Fig. 29. Horizontal section at the level of the anterior commissure.

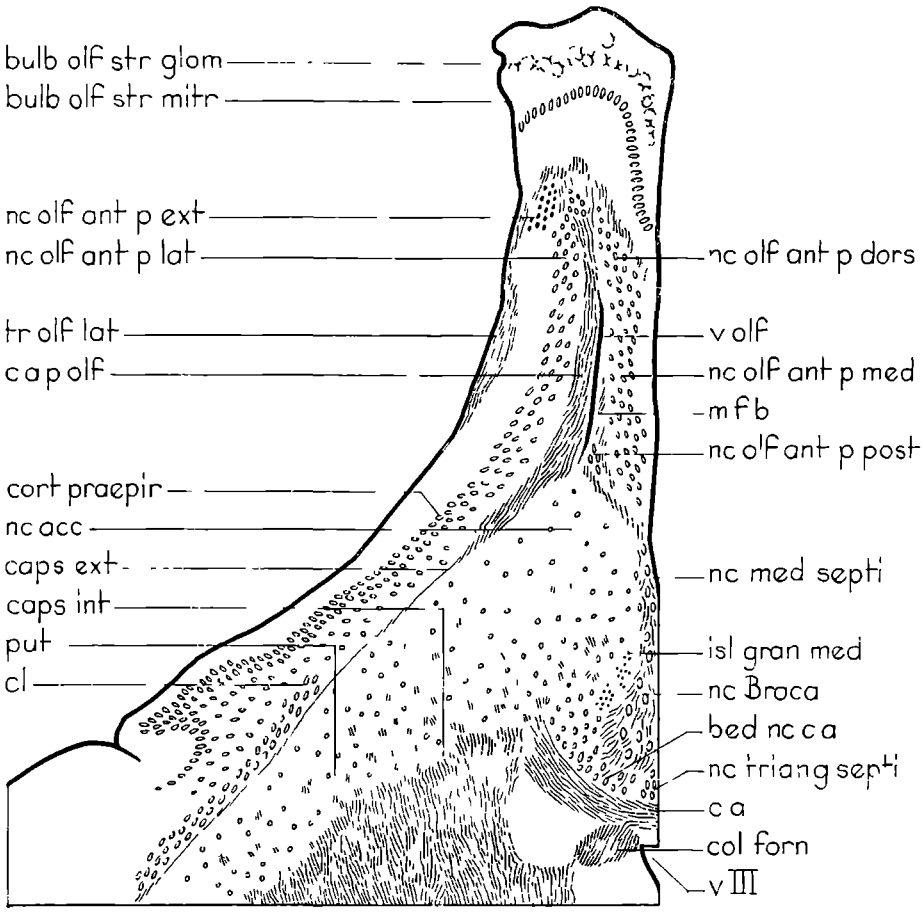

bulb olf str glom
bulb olf str mitr
nc olf ant p ext
nc olf ant p lat
tr olf lat
c a p olf
cort praepir
nc acc
caps ext
caps int
put
cl
nc olf ant p dors
v olf
nc olf ant p med
m f b
nc olf ant p post
nc med septi
isl gran med
nc Broca
bed nc c a
nc triang septi
c a
col forn
v III

Fig 29

Fig 30 Horizontal section at the level of the pars ventralis of the anterior olfactory nucleus

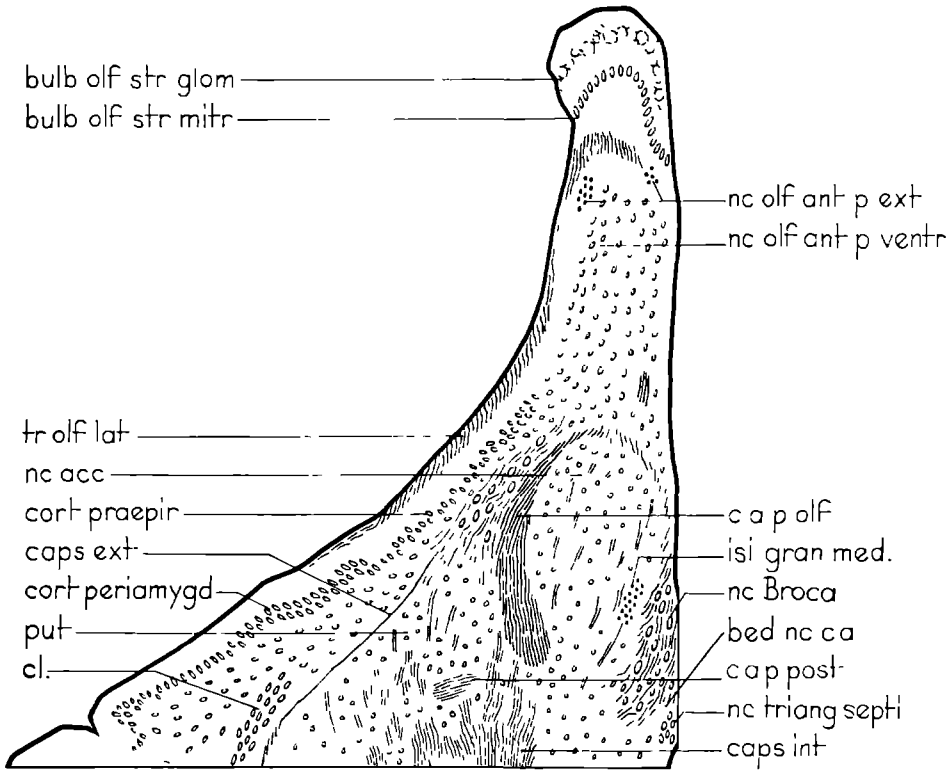

bulb olf str glom
bulb olf str mitr
nc olf ant p ext
nc olf ant p ventr
tr olf lat
nc acc
cort praepir
caps ext
cort periamygd
put
cl
c a p olf
isi gran med.
nc Broca
bed nc c a
c a p post
nc triang septi
caps int

Fig. 30

Fig 31. Horizontal section through the dorsal part of the tuberculum olfactorium

Fig 32 Horizontal section through the ventral part of the tuberculum olfactorium

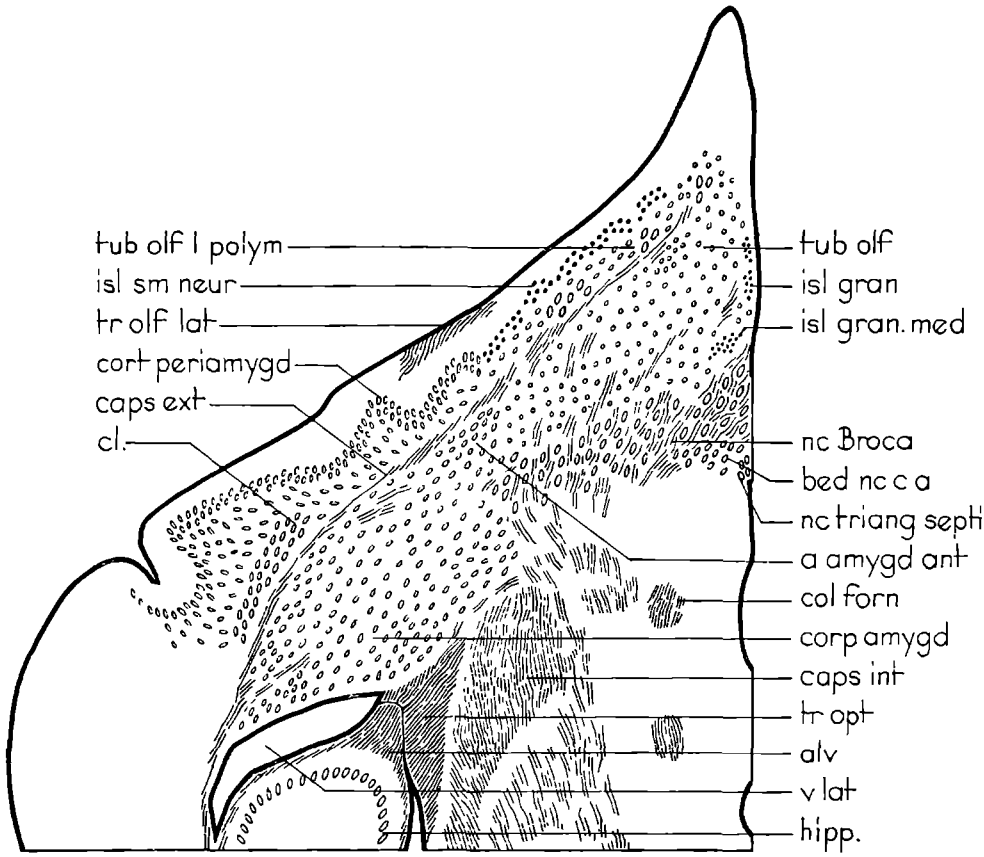

tub olf l polym
isl sm neur
tr olf lat
cort periamygd
caps ext
cl.
tub olf
isl gran
isl gran. med
nc Broca
bed nc c a
nc triang septi
a amygd ant
col forn
corp amygd
caps int
tr opt
alv
v lat
hipp.

Fig. 31

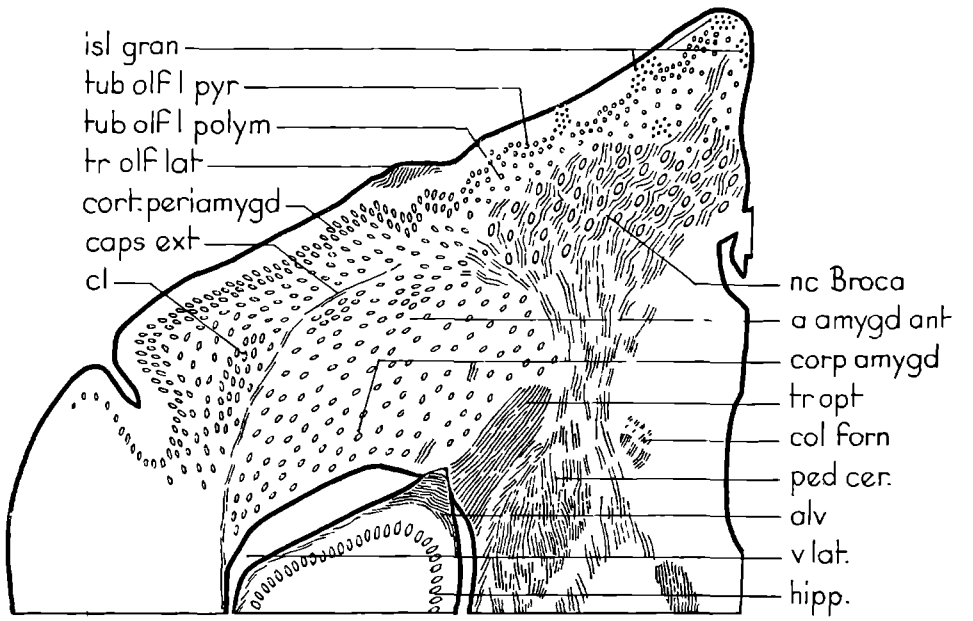

isl gran
tub olf l pyr
tub olf l polym
tr olf lat
cort: periamygd
caps ext
cl
nc Broca
a amygd ant
corp amygd
tr opt
col forn
ped cer.
alv
v lat.
hipp.

Fig. 32

Fig 33 Horizontal section at the level of the optic chiasma.

Fig 34 Horizontal section at a level slightly ventral to the optic chiasma.

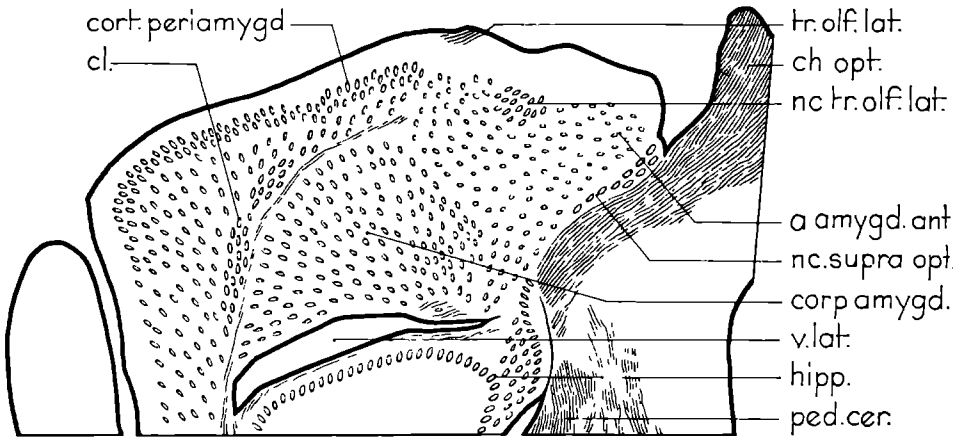

cort: periamygd
cl.
tr. olf: lat.
ch opt:
nc tr. olf: lat.
a amygd. ant.
nc. supra opt.
corp amygd.
v. lat:
hipp.
ped. cer.

Fig. 33

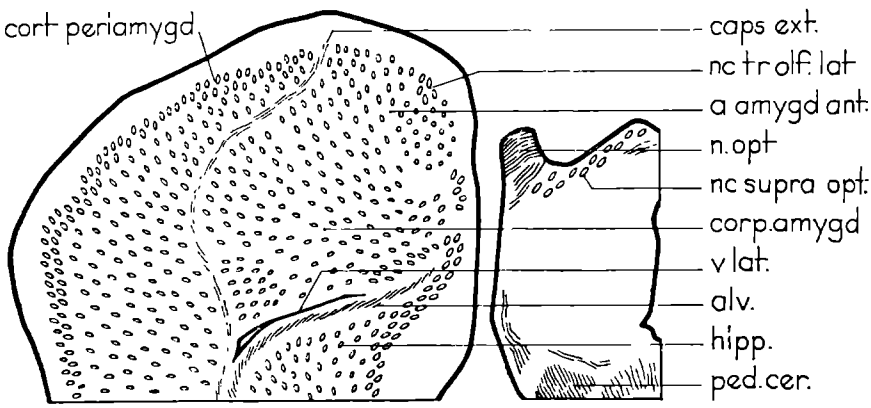

cort periamygd
caps ext.
nc tr olf: lat
a amygd ant:
n. opt
nc supra opt:
corp. amygd
v lat:
alv.
hipp.
ped. cer.

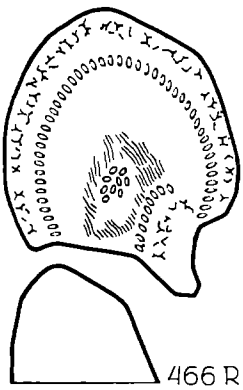
Fig. 34

Figs 35-43 Drawings of horizontal sections of nucleus olfactorius anterior pars rostralis in divers guinea pig brains
Kluver-Barrera method Magnification 14 ×
The sections of each series are numbered from dorsal to ventral

Fig 35 Series 320, adult guinea pig, right side, 10 μ

Fig 36 Series 333, 11 days old guinea pig, right side, 15 μ

Fig 37 Series 353, 17 days old guinea pig right side 10 μ



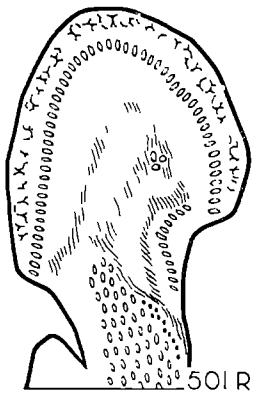


Fig 35

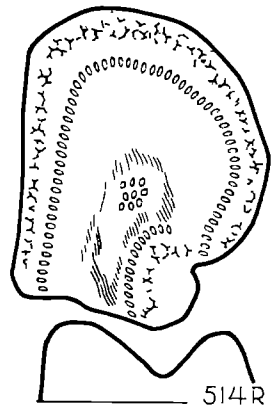
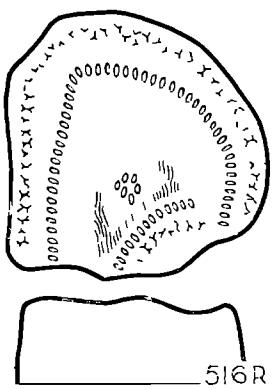
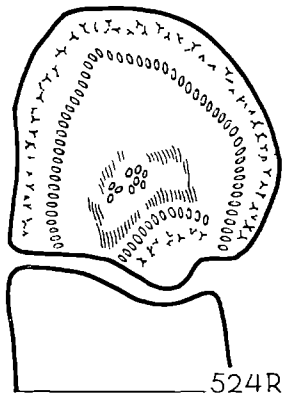
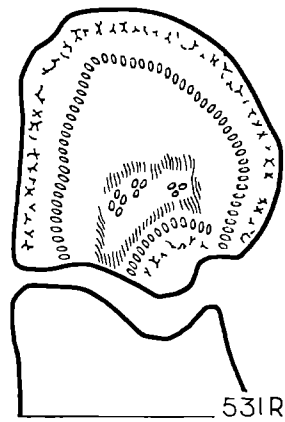


Fig 36







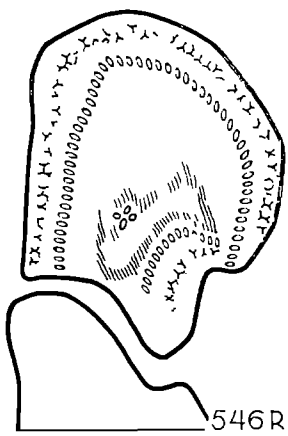


Fig 37

Fig. 38. Series 325, 7 days old guinea pig, right side, 10 μ.

Fig. 39. Series 322, adult guinea pig, right side, 10 μ.

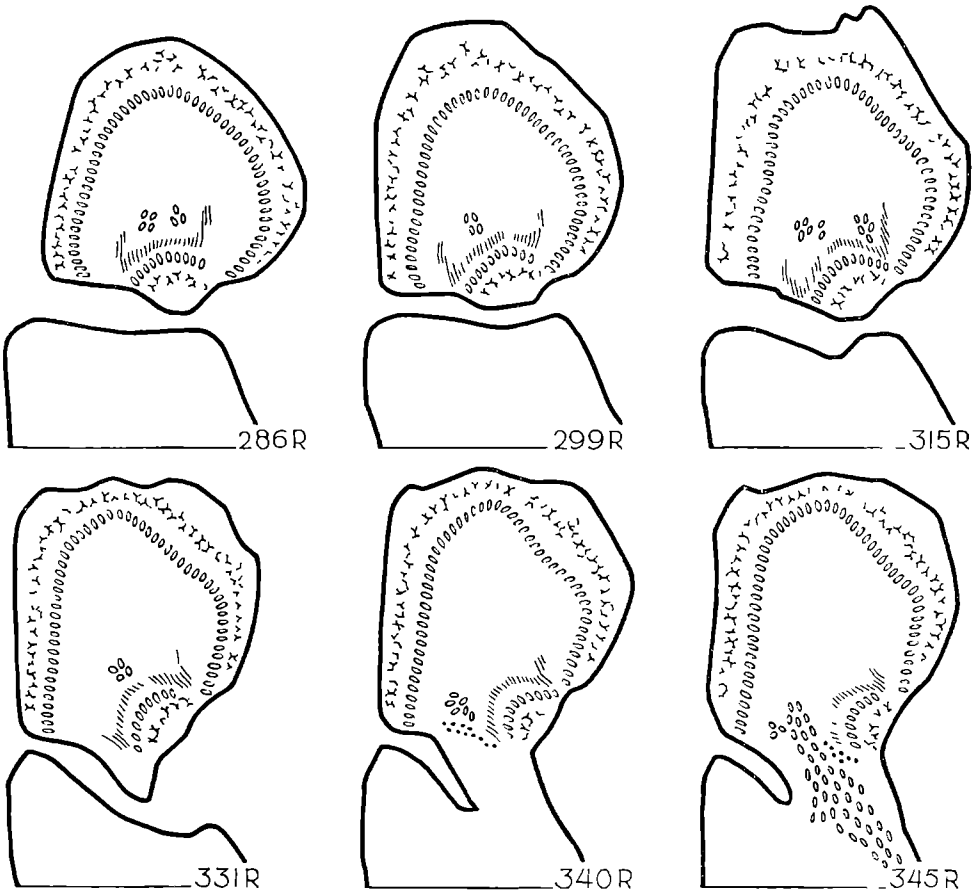


Fig 38

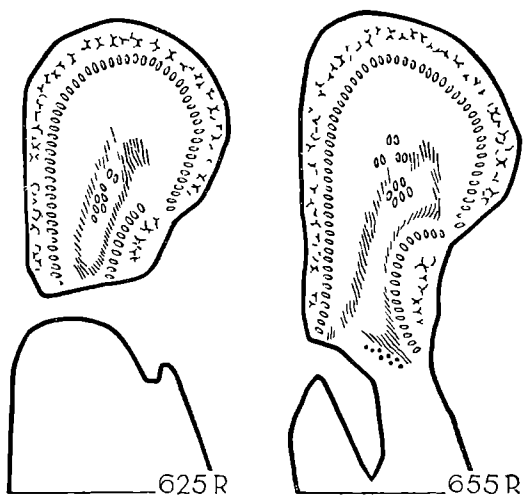
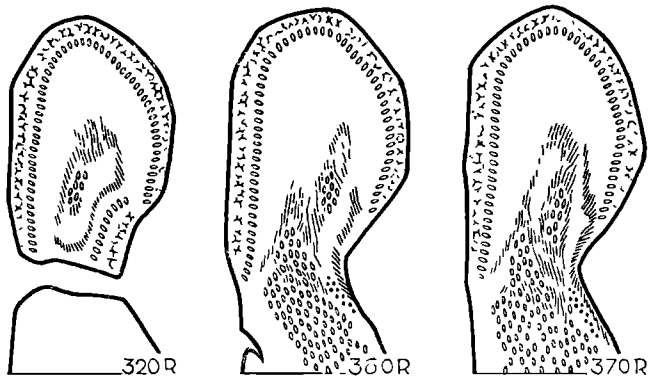


Fig 39

Fig 40 Series 319, adult guinea pig, right side 10 μ

Fig 41 Series 319, adult guinea pig, left side, 10 μ



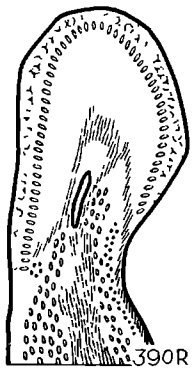
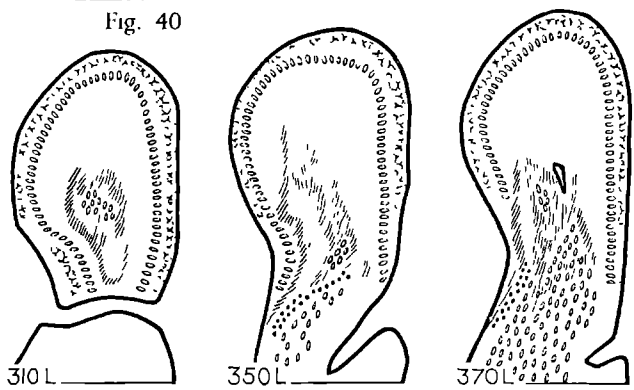


Fig. 40



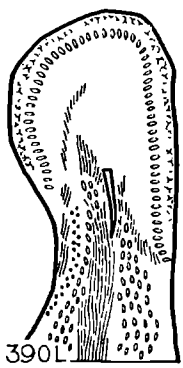
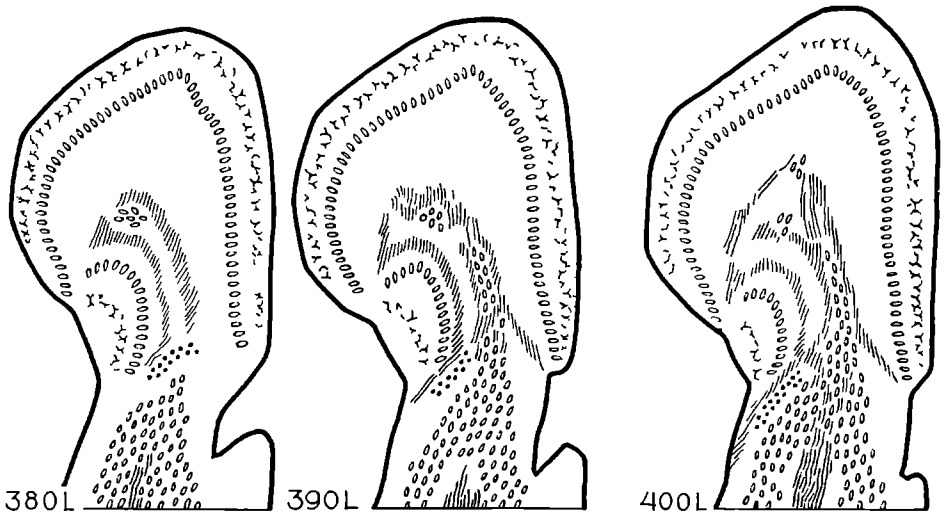


Fig 41

Fig 42 Series 329, adult guinea pig left side, 10 μ

Fig 43 Series 329, adult guinea pig, right side, 10 μ



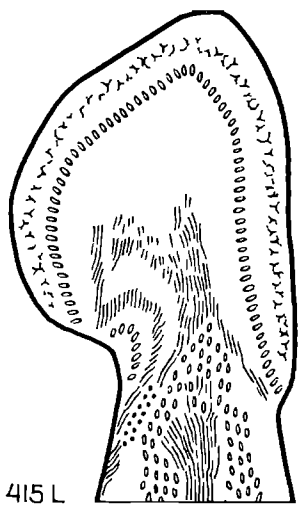
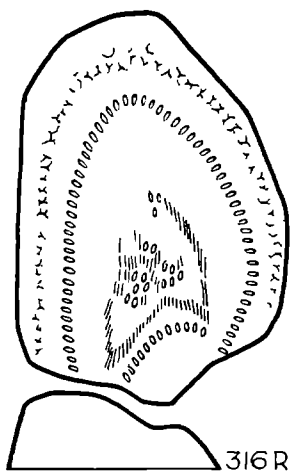


Fig 42



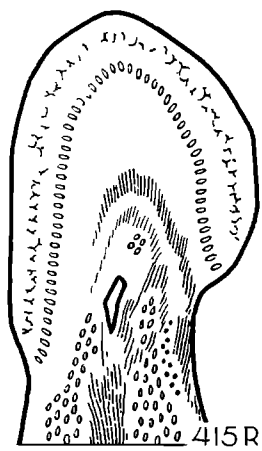
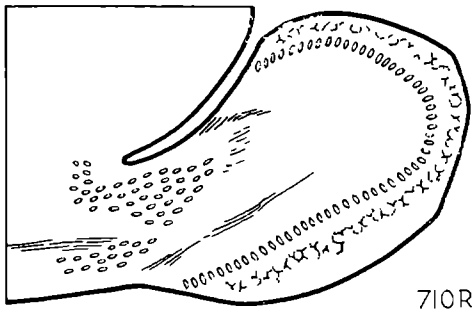
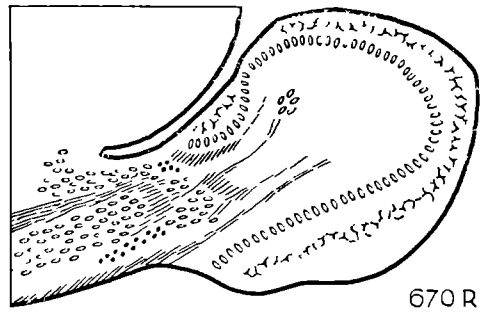
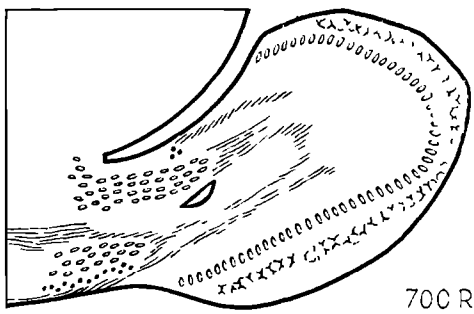


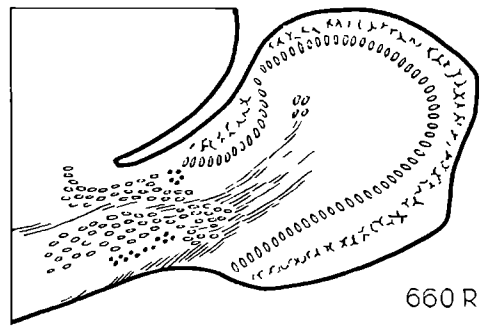
Fig 43

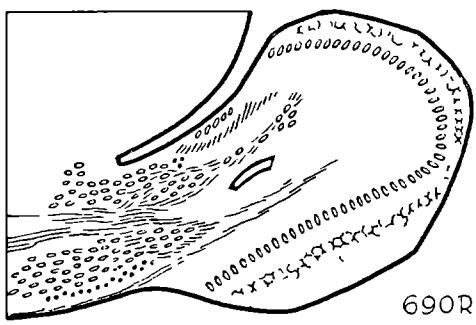
Fig 44 Drawings of sagittal sections of right nucleus olfactorius anterior of an adult guinea pig
Series 378 Kluver-Barrera method 10 μ Magnification 14 $\times$
The sections are numbered from lateral to medial.











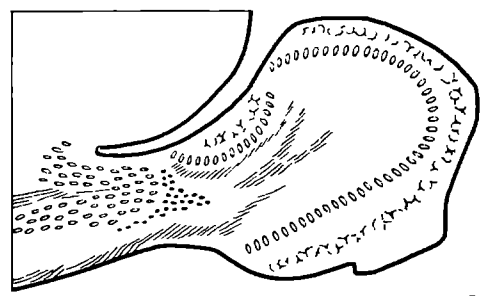
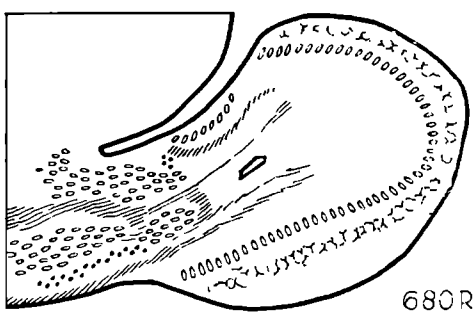


Fig 44



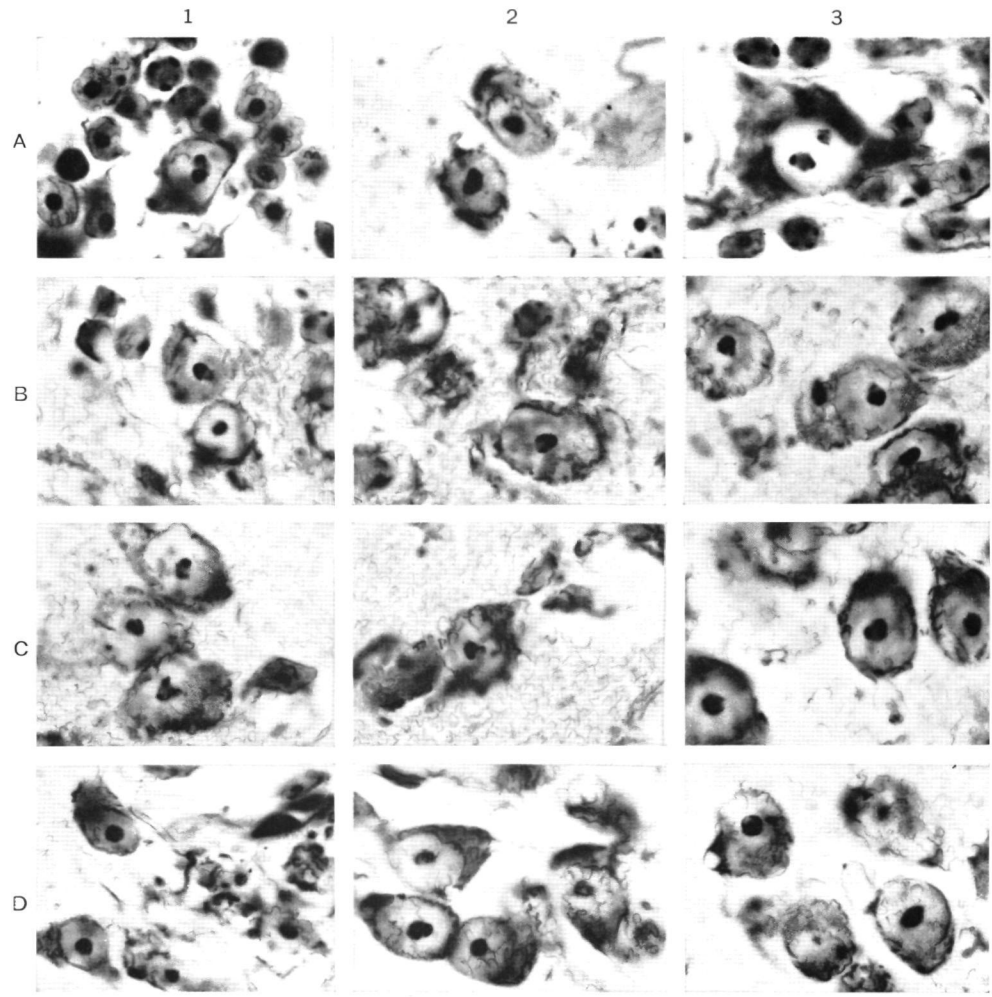


Fig. 45. Photomicrographs showing divers neurons of the anterior olfactory lobe. Klüver-Barrera method. Magnification 750 ×.
A 1. Bulbus olfactorius, interstitial tufted cell and external granular cells. A 2. Bulbus olfactorius, internal tufted cells. A 3. Bulbus olfactorius, mitral cell. B 1. Bulbus olfactorius accessorius, tufted cells. B 2. Nucleus olfactorius anterior, pars rostralis. B 3. Nucleus olfactorius anterior, pars lateralis. C 1. Nucleus olfactorius anterior, pars medialis. C 2. Nucleus olfactorius anterior, pars ventralis. C 3. Nucleus olfactorius anterior, pars posterior. D 1. Nucleus olfactorius anterior, pars externa. D 2. Cortex praepiriformis, pyramidal cell layer. D 3. Tuberculum olfactorium, pyramidal cell layer.

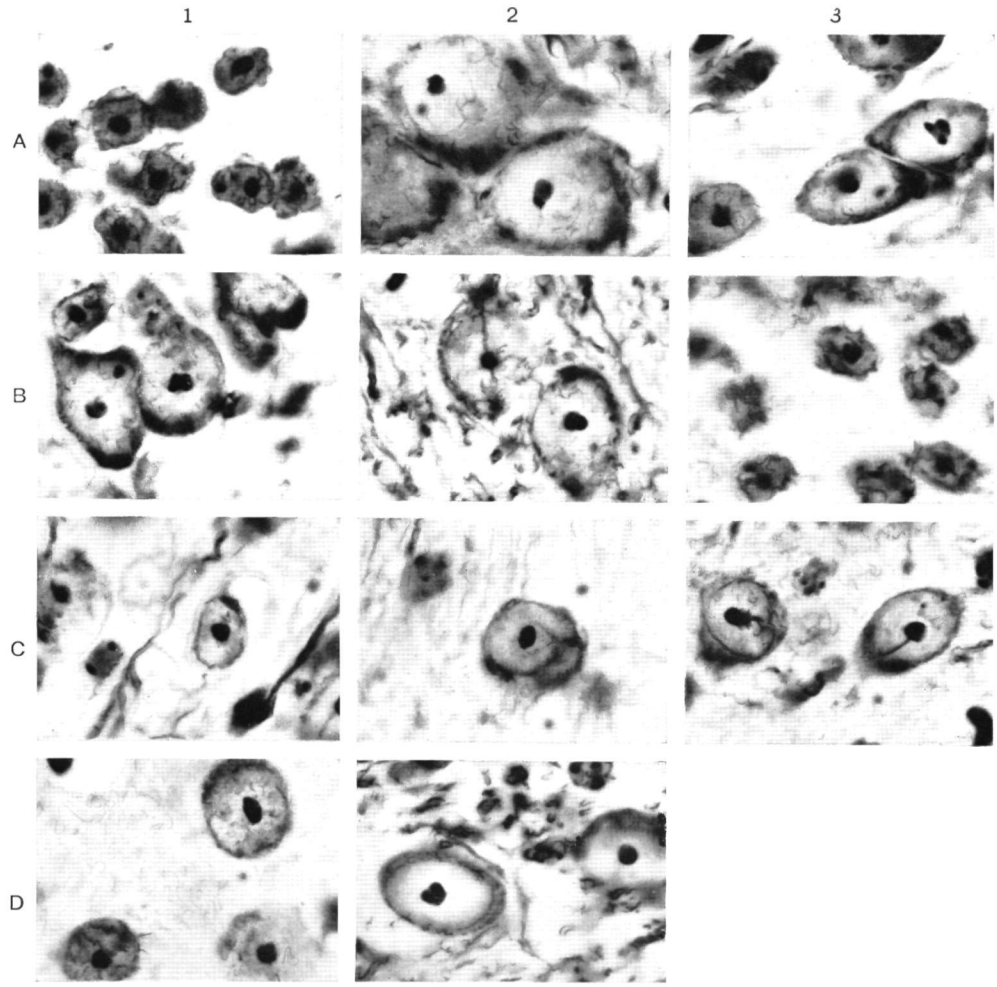


Fig. 46. Photomicrographs showing divers neurons of the anterior olfactory lobe. Klüver-Barrera method. Magnification 750 ×.
A 1. Tuberculum olfactorium, island of small neurons. A 2. Nucleus of Broca. A 3. Nucleus hippocampi anterior. B 1. Nucleus septohippocampalis. B 2. Nucleus medialis septi. B 3. Bed nucleus of the commissura fornicis. C 1. Nucleus triangularis septi. C 2. Bed nucleus of the commissura anterior. C 3. Nucleus lateralis septi. D 1. Nucleus accumbens. D 2. Nucleus septalis fimbrialis.

The connections of the main and accessory olfactory bulb and of the anterior olfactory nucleus

Lateral olfactory Tract, anterior commissure and medial forebrain bundle

The investigation of the connections of the main and accessory olfactory bulb and of the anterior olfactory nucleus in the guinea pig, executed by means of degeneration experiments, will be described in this chapter

Since in 1870 Gudden made the first experimental anatomical investigation into the efferent projection of the olfactory bulb numerous investigators have occupied themselves with the connections of the olfactory bulb and anterior olfactory nucleus

As to the secondary olfactory connections, it has always been a point of controversy whether there exists a commissural component in the projection of the olfactory bulb apart from the lateral olfactory tract

Whereas Loewenthal (1897), van Gehuchten (1904) and Young (1941, 1942) could only observe degenerated fibres in the anterior commissure when in addition to the olfactory bulb also the olfactory peduncle was injured, other authors including Probst (1901), Cajal (1911), Le Gros Clark and Meyer (1947) and Adey (1953) did report degeneration in the anterior commissure after removal of the olfactory bulb without injury to the peduncle

The latter authors, using the silver impregnation method of Glees (1946), noticed not only termination of these commissural fibres in the heterolateral olfactory bulb, but also in the more centrally situated central amygdaloid nucleus and bed nucleus of the stria terminalis, both homo- and heterolaterally

About the efferent connections of the accessory olfactory bulb only the experiments of Allison (1953 a) and Johnson (1959) provide data Both authors came to the conclusion that the tufted cell axons of the accessory bulb pass into the lateral olfactory tract

According to the experiments of Loewenthal, van Gehuchten and Young, as reported above, and to those of Brodal (1948), Allison (1953 a) and Johnson (1959) the anterior olfactory nucleus and probably only the pars dorsalis of this nucleus contributes fibres to the

anterior limb of the anterior commissure However, no unanimity of opinions exists about the termination of these commissural fibres Concerning the connections of the other portions of the anterior olfactory nucleus no reports could be found in the literature.

In view of these data it seemed to us of interest to examine again the connections of the main and accessory olfactory bulb and of the anterior olfactory nucleus in a mammal using a silver impregnation method.

Except in the bulbar and retrobulbar area, lesions were also made in other parts of the anterior olfactory lobe for obtaining additional data about the origin, course and termination of the fibre systems which make up the white matter of the anterior olfactory lobe. the lateral olfactory tract, anterior commissure and medial forebrain bundle.

Material and methods

In 14 young and 26 adult guinea pigs (Cavia porcellus) unilateral surgical and electrolytic lesions were made in the anterior olfactory lobe. A small part of the skull roof was removed and an incision was made in the dura mater. The surgical lesions were made with a sharp fine-bladed, sometimes heated, scalpel.

All operations were conducted under nembutal anaesthesia administered by intraperitoneal route After survival times, varying from 3 to 48 days, the animals were perfused, under nembutal anaesthesia, with 10% formol-saline (60 ml per kg of bodyweight). After at least six hours the brains were removed, during some weeks immersed in 10% formalin and subsequently sectioned frontally, horizontally or sagittally.

Methods

The paraffin and frozen sections, 10 and 25 μ thick respectively, were stained according to the methods of Kluver and Barrera (1953), Nauta (1950), Nauta and Gygax (1954) and the modified Nauta-Gygax method (Nauta, 1957).
In order to be suitable to frozen as well as to paraffin sections, the original Nauta method (Nauta, 1950) was modified by us as follows:

For paraffin sections:

1. Remove the paraffin with xylene and take the sections through the alcohols to distilled water Leave the sections in several changes of distilled water for some hours.
2. Place for 4 hours at 56° C in the following solution:
   280 ml. silver nitrate 1.5%
   14 ml. pyridine
   4 ml borax 1 9%
   16 ml. boric acid 1.24%
   The Ph of this buffered solution is 7.8.
3. Without washing place the sections for 2 min. in:
   180 ml. silver nitrate 1 5%
   48 ml absolute alcohol

Just before using add
6 ml concentrated ammonia
6 ml ammonium hydroxide 2 5%
Shake vigorously

4 Transfer the sections for 10 sec to a reducing fluid, composed of
180 ml distilled water
20 ml absolute alcohol
6 ml citric acid 1%
6 ml formalin 10%
Shake vigorously

5 Without washing place the sections for 2 min in
200 ml distilled water
10 ml citric acid 1%

6 Wash thoroughly in distilled water, dehydrate in alcohol, clear in xylol and mount in caedax

If frozen sections are used, they are mounted prior to staining and placed overnight in the buffered silver nitrate solution at 21° C in the dark Otherwise the procedure is the same as that for paraffin sections

For establishing, in degeneration experiments by means of silver impregnation methods, a connection between two or more cell groups in the central nervous system, it is essential in our opinion, after having destroyed the cells of origin or having transected the fibre bundle or bundles connecting the cell groups, to demonstrate not only terminal or preterminal degeneration but also orthograde degeneration of the stem fibres The same approach has been taken by Nauta (Glees and Nauta, 1955) "It is only by the process of tracing axon degeneration distally that the terminal distribution of many fibre systems can be definitely ascertained '

We, therefore in our study preferred the Nauta techniques to the Glees method, because the former methods were developed to bring out the pathological changes more or less selectively and to suppress the normal fibre patterns (Glees and Nauta, 1955) Besides, in our laboratory the Glees method never gave satisfactory impregnation of degenerating fibres and preterminals as compared with the Nauta methods Although in the original Nauta method a smaller proportion of normal nerve fibres remains unstained than with the newer methods, it has the advantage to be suitable in our modification to paraffin embedded material

Beside the silver staining methods we have used the combined cell and myelin impregnation of Kluver and Barrera, of which the use for the experimental tracing of fibre connections in the central nervous system for the first time was demonstrated by Lammers (1957) According to this author the Kluver-Barrera method can be used in frozen as well as in celloidin and paraffin sections By our experience the paraffin sections give the best results

The serial paraffin sections in our experiments were alternatively stained by the Kluver-Barrera method and by our modification of the original Nauta method This made it possible

to study and compare with each other in one series the myelinsheath and axon degeneration Moreover, the Kluver-Barrera stain facilitates identification of the several nuclear masses and fibre systems, essential for defining precisely the position of the lesions made and for determining the course and termination of degenerated fibres

In sections stained with the Nauta method the axonal degeneration of the stem fibres presents itself as rows of drop-like formations Using the modified original Nauta method we experienced that after bulbar ablation in the area of distribution of the lateral olfactory tract also a degeneration characterized by an inorderly arrangement of very fine light-brown droplets occurs (fig 53) In accordance with Bowsher et al (1960) we have called this phenomenon "preterminal degeneration", reservating the term "terminal degeneration" only for degenerating terminal boutons and the very fine fibres leading up to them, which structures are, however, not demonstrable by the Nauta techniques The same type of degeneration is reported by Blackstad (1956) and White (1959) in Nauta (1950) preparations of the hippocampal formation Probably as a result of the preliminary treatment to suppress the impregnation of normal fibres the Nauta-Laidlaw method, as White observed in his material, fails to impregnate these fine degeneration products

In sections stained with the Kluver-Barrera method the degeneration presents itself as a disintegration of the myelinsheath together with the appearance of globules of deep blue staining myelinsubstance In adult guinea pigs the first signs of degenerating myelinsheaths are visible after three postoperative days in the vicinity of the lesion After five days the affected fibre bundle shows degeneration along its whole length In a four days old animal the latter was already the case after a survival time of three days

Material

The lesions made can be classified as follows

1 Lesions in the main and accessory olfactory formations
2 Lesions in the anterior olfactory nucleus
3 Lesions elsewhere in the anterior olfactory lobe

Lesions in the main and accessory olfactory formations

In 5 young and 15 adult guinea pigs (B 1-B 20, survival times 3-30 days) lesions were made in the bulbar area which were strictly confined to the olfactory and accessory olfactory formations Eight experiments have been selected as the best ones for the study of the secondary olfactory connections

Guinea pig B 1 (S 308) Adult Survival time 5 days The olfactory bulb is almost totally ablated Laterally the lesion comprises the granular cell layer of the accessory olfactory bulb The cell groups of the nucleus olfactorius anterior pars rostralis are not destroyed (fig 47)

Guinea pig B 2 (S 332) Adult Survival time 10 days The anterior one-third of the olfactory bulb is ablated (fig 47) Frozen sections

Guinea pig B 3 (S 307) Adult Survival time 6 days The anterolateral part of the olfactory bulb is ablated The lesion does not comprise the accessory olfactory bulb and the cell groups of the nucleus olfactorius anterior pars rostralis

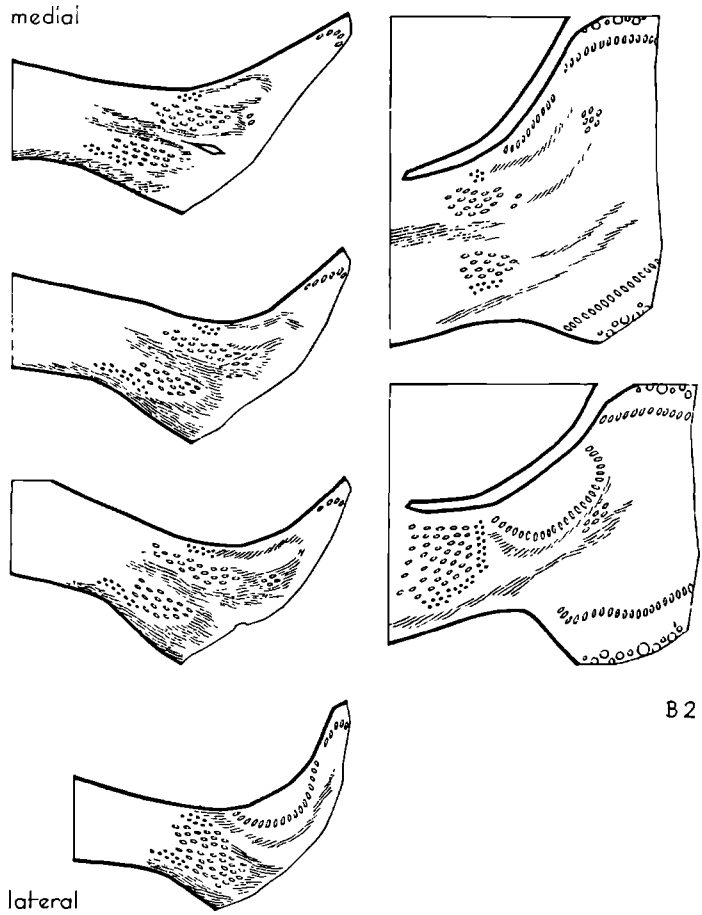


Fig. 47. Two lesions of the olfactory formation. Sagittal sections.

Guinea pig B 4 (S. 394). Adult. Survival time: 7 days. In this animal a stab in the olfactory bulb was made from the dorsal side by means of a small spatula. This proved to result in an oblong lesion just anterior to the nucleus olfactorius anterior pars rostralis. Frozen sections.

Guinea pig B 5 (S. 325). 4 days old. Survival time: 3 days. The anterior one-third of the olfactory bulb is ablated (fig. 48).

Guinea pig B 6 (S. 363). 7 days old. Survival time: 6 days. A lesion dorsolaterally in the olfactory bulb. The cell groups of the nucleus olfactorius anterior pars rostralis and the accessory olfactory bulb are not involved (fig. 48).

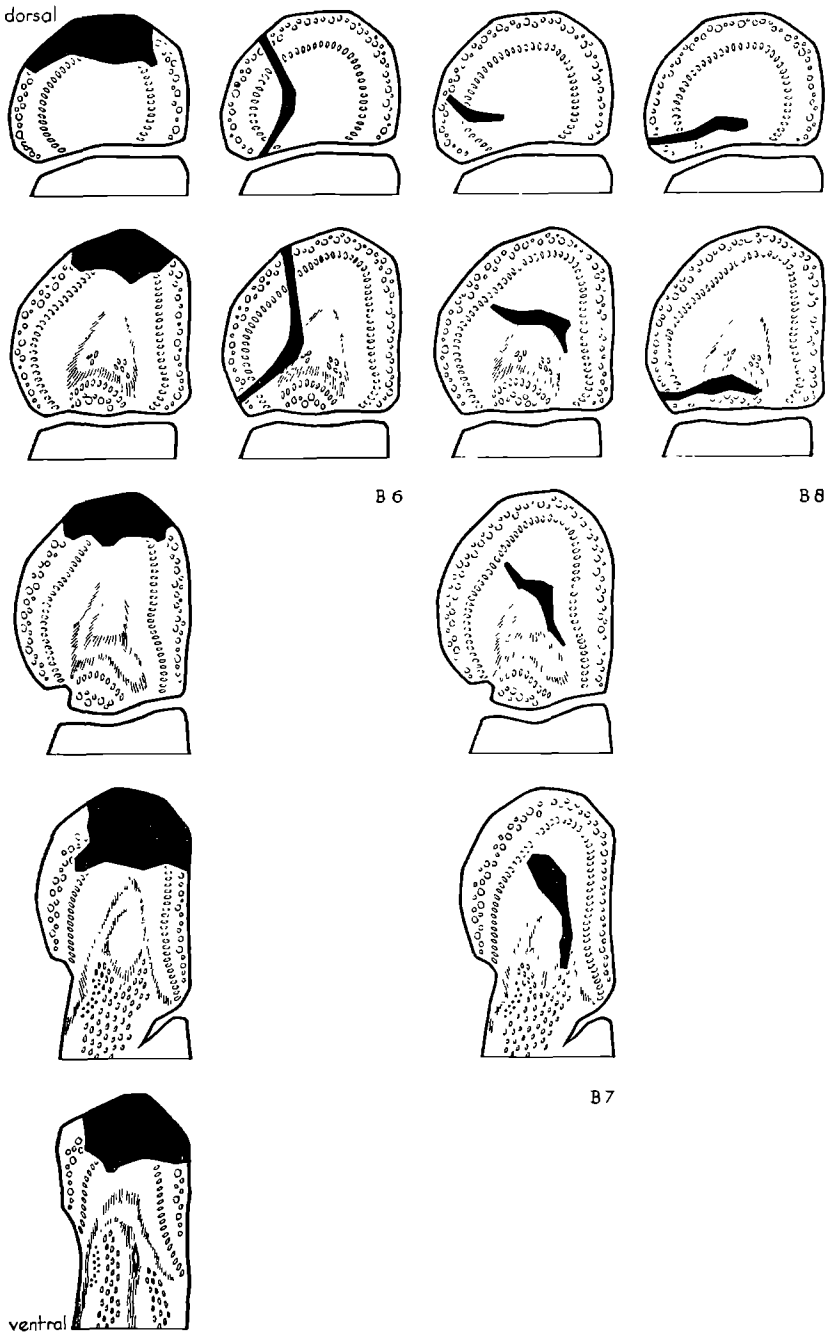


Fig. 48. Standarized diagram of three lesions in the main olfactory formation and of one lesion in the accessory olfactory formation. Horizontal sections.

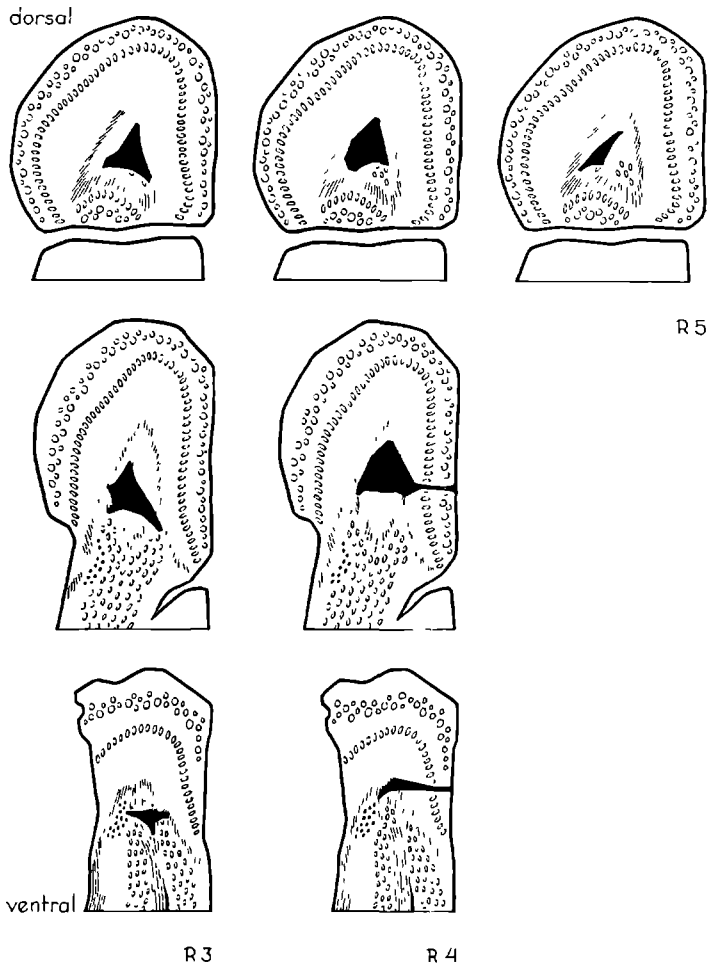


Fig. 49. Standarized diagram of three lesions of the nucleus olfactorius anterior pars rostralis. Horizontal sections.

Guinea pig B 7 (S 336). Adult Survival time: 6 days A lesion in the middle of the dorsal part of the olfactory bulb, anterior to the nucleus olfactorius anterior pars rostralis (fig. 48).

Guinea pig B 8 (S. 376). Adult. Survival time: 14 days. A lesion dorsally in the accessory olfactory bulb, involving all layers The nucleus olfactorius anterior pars rostralis is not destroyed (fig 48).

Lesions in the anterior olfactory nucleus

Guinea pig R 1 (S 330) 5 days old Survival time 21 days A lesion dorsally in the bulbar area, destroying the dorsolateral part of the accessory olfactory bulb and the cell groups of the anterior olfactory nucleus pars rostralis

Guinea pig R 2 (S 342) 13 days old Survival time 40 days A small lesion dorsally in the olfactory bulb comprising the cell groups of the nucleus olfactorius anterior pars rostralis

Guinea pig R 3 (S 343) 13 days old Survival time 48 days The lesion occupies the olfactory bulb just rostral to the accessory bulb Dorsally it destroys the nucleus olfactorius anterior pars rostralis Ventrally it encroaches upon the pars lateralis and pars externa (fig 49)

Guinea pig R 4 (S 331) 8 days old Survival time 36 days A lesion caudally in the olfactory bulb destroying the lateral cell groups of the nucleus olfactorius anterior pars rostralis (fig 49)

Guinea pig R 5 (S 339) 10 days old Survival time 6 days The lesion in the dorsocaudal part of the olfactory bulb involves part of the lateral cell group of the nucleus olfactorius anterior pars rostralis (fig 49) Frozen sections

Guinea pig D 1 (S 374) Adult Survival time 14 days The lesion comprises from dorsal to ventral the most caudal part of the main olfactory bulb the accessory bulb and the nucleus olfactorius anterior pars dorsalis

Guinea pig D 2 (S 373) Adult Survival time 14 days The lesion occupies the caudal part of the nucleus olfactorius anterior pars dorsalis Medially the most medial fibres of the anterior limb of the anterior commissure are interrupted Dorsally the lesion comprises the tip of the frontal lobe of the hemisphere ventrally it extends as far as the nucleus olfactorius anterior pars ventralis

Guinea pig D 3 (S 371) Adult Survival time 14 days The lesion in the olfactory bulb extends from dorsorostral to ventrocaudal It destroys the nucleus olfactorius anterior pars dorsalis and the rostral tip of the pars lateralis Probably part of the pars externa is included in the lesion (fig 50)

Guinea pig L 1 (S 351) 9 days old Survival time 15 days A lesion at the transition from the olfactory bulb to the peduncle The lateral olfactory tract and the anterior limb of the anterior commissure are transected The lesion involves the nucleus olfactorius anterior pars externa and the rostral part of the pars lateralis

Guinea pig L 2 (S 350) 9 days old Survival time 8 days A lesion caudally in the bulbar area and at the transition from the bulb to the olfactory peduncle Dorsally it involves the granular cell layer of the accessory bulb ventrally it destroys the nucleus olfactorius anterior pars externa and the rostral part of the pars lateralis (fig 50)

Guinea pig M 1 (S 329) Adult Survival time 10 days A lesion in the posterior part of the nucleus olfactorius anterior pars medialis medial to the anterior limb of the anterior commissure The medial forebrain bundle is interrupted by the lesion

Lesions elsewhere in the anterior olfactory lobe

Guinea pig O 1 (S 379) Adult Survival time 14 days The anterior limb of the anterior commissure is transected just behind the olfactory peduncle by means of a fine-bladed scalpel Dorsally the fibres of the external and internal capsules are interrupted Ventrally the lesion extends into the posterior part of the olfactory tubercle and the lateral part of the nucleus of Broca A process of softening has taken place in the capsula interna and more ventrally in the lateral hypothalamic area where it communicates with the lesion

Guinea pig O 2 (S 375) Adult Survival time 14 days The anterior limb of the anterior commissure is transected by means of a fine-bladed scalpel at approximately the same place as in the preceding case Ventrally the lesion extends into the lateral part of the olfactory tubercle (fig 51)

Guinea pig O 3 (S 352) 11 days old Survival time 20 days A small electrolytic lesion laterally in the decussation of the anterior commissure The posterior limb and the pars ad striam terminalem of the commissure are not involved

Guinea pig O 4 (S 380) Adult Survival time 14 days A lesion laterally in the olfactory

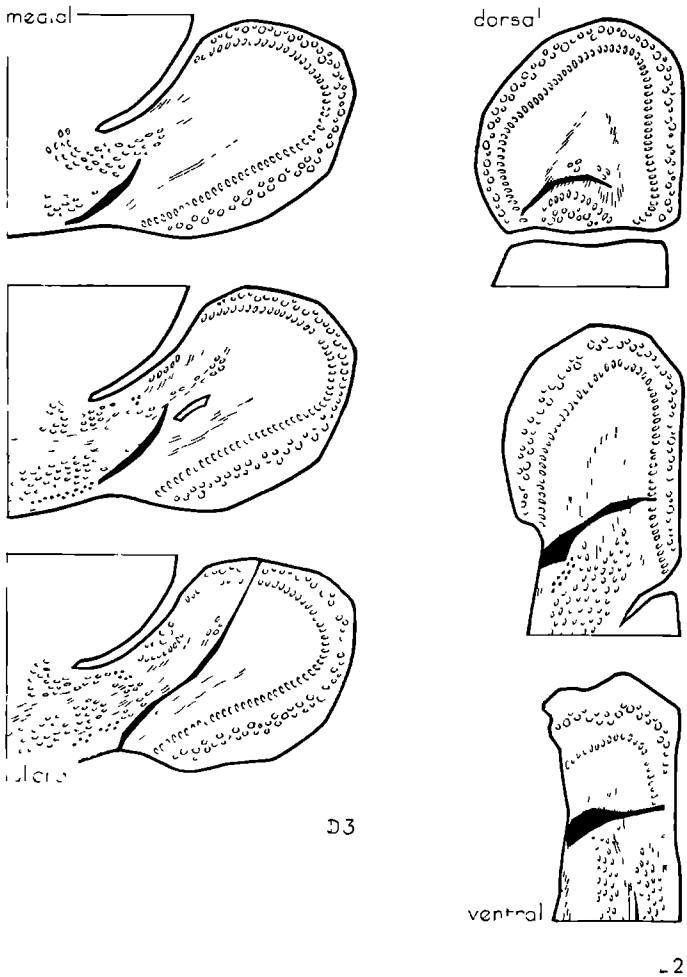


Fig. 50 Two lesions at the transition from the bulbar to the retrobulbar area. Sagittal (on the left) and horizontal sections.

peduncle, destroying the posterior part of the nucleus olfactorius anterior pars lateralis. Laterally the lesion extends into the lateral olfactory tract, medially into the plexiform layer between the nucleus olfactorius anterior pars posterior and the nucleus accumbens. Only the lateral fibers of the anterior limb of the anterior commissure are interrupted (fig. 51).

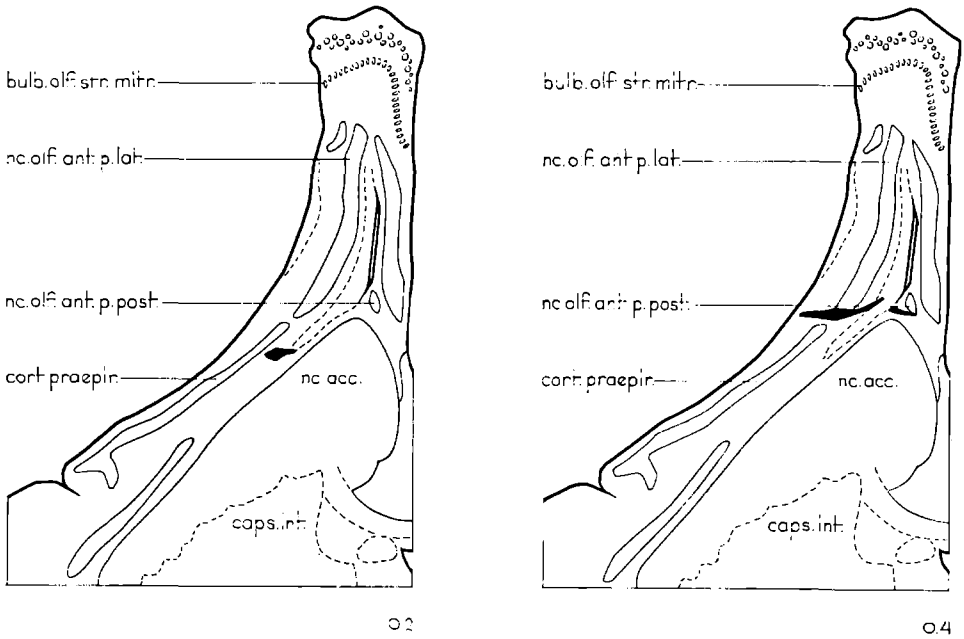


Fig. 51. Two horizontal sections illustrating a lesion caudal to and a lesion caudally in the olfactory peduncle. A list of abbreviations is given on p. 28, 29

Guinea pig O 5 (S. 377). Adult. Survival time: 14 days. A small lesion in the posterior part of the nucleus olfactorius anterior pars lateralis at the transition to the prepiriform cortex, lateral to the anterior limb of the anterior commissure. The lesion interrupts the most dorsal fibres of the lateral olfactory tract.

Guinea pig O 6 (S. 389). Adult. Survival time: 13 days. An electrolytic lesion in the prepiriform cortex and in the anterolateral part of the olfactory tubercle. The lateral olfactory tract is involved. The lesion and the electrode track are lateral to the anterior limb of the anterior commissure.

Guinea pig O 7 (S. 370). Adult. Survival time: 14 days. A scalpel was passed downward and slightly backward from above in the rostral part of the nucleus accumbens and the olfactory tubercle, transecting the fibre bundles of the medial forebrain bundle. Ventrally the lesion reaches the ventral surface of the hemisphere. Laterally the most medial fibres of the anterior limb of the anterior commissure are interrupted in their course.

Guinea pig O 8 (S. 353). 11 days old. Survival time: 6 days. An electrolytic lesion in the area septalis. From dorsal to ventral the lesion comprises: the nucleus medialis septi, the nucleus of Broca and the bed nucleus of the commissura anterior (fig. 52).

Guinea pig O 9 (S. 372). Adult. Survival time: 14 days. A scalpel was passed downward and slightly backward and lateralward from the convexity of the left cerebral hemisphere through the genu of the corpus callosum. The nucleus septohippocampalis and the rostral part of the nucleus medialis septi are destroyed by a hemorrhage. The lesion extends as a narrow slit caudally in the nucleus accumbens and olfactory tubercle as far as the ventral surface of the brain.

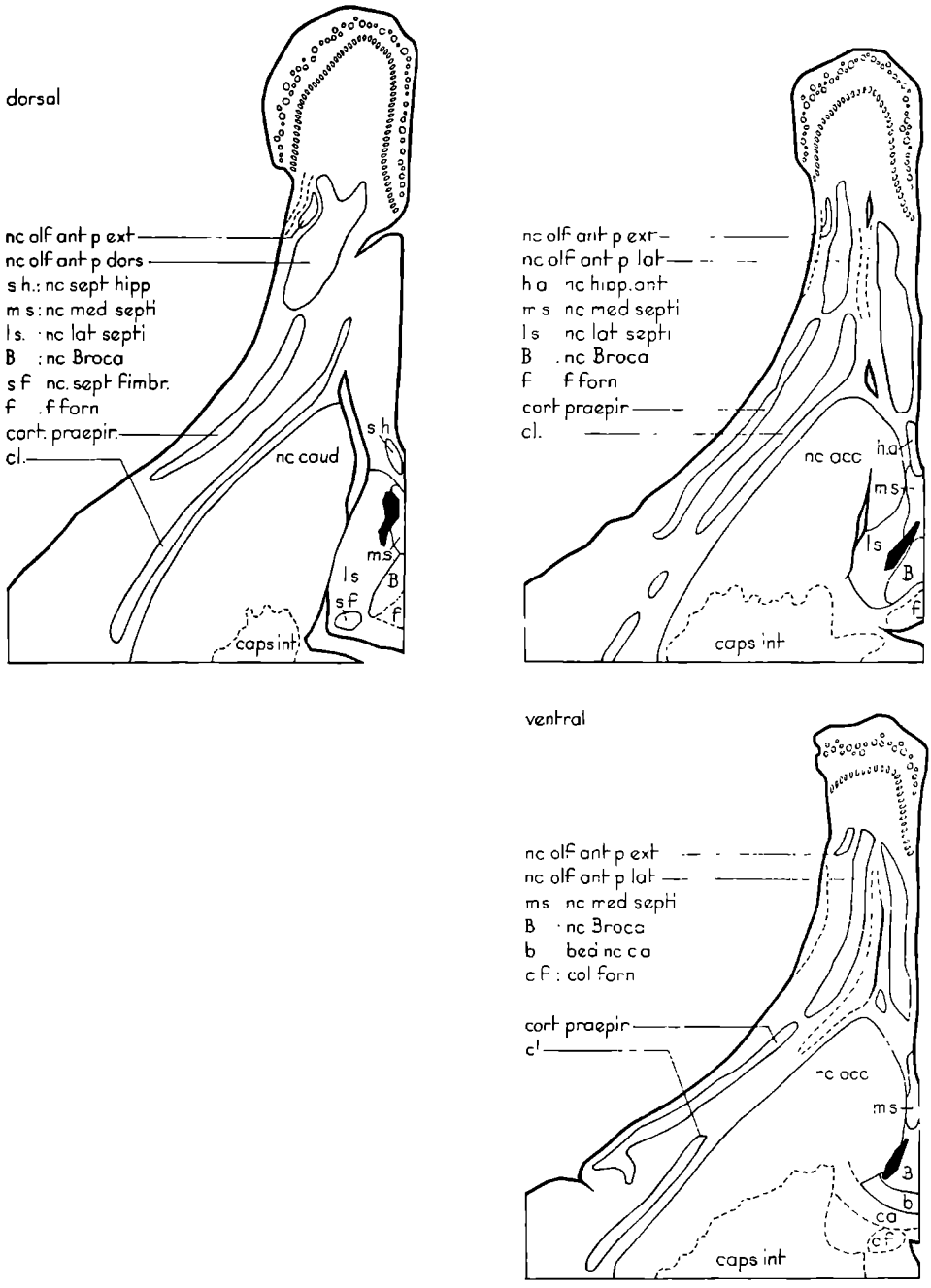


Fig. 52. Standarized diagram of an electrolytic lesion in the area septalis. Horizontal sections. A list of abbreviations is given on p. 28, 29

Survey of the experimental anatomical studies of the connections of the olfactory bulb and anterior olfactory nucleus in mammals. Lateral olfactory tract, anterior commissure and medial forebrain bundle

The greater part of the experimental anatomical studies of the connections of the olfactory bulb and anterior olfactory nucleus in mammals is made with the Marchi method and that by Loewenthal (1897), Probst (1901), van Gehuchten (1904), Cajal (1901, 1911) and Young (1941, 1942) in the rabbit, by Fox and Schmitz (1942, 1943) in the cat, by Fox, Fisher and Desalva (1948) in Macaca mulatta and by Morin (1950) in the guinea pig

In the rabbit Gudden (1870), Ganser (1879, 1882) and Winkler (1917, 1918) made use of the atrophy method, for the first time applied by Gudden, while Brodal (1948) in the white rat and Allison (1953 a) in the rabbit and rat applied the modified Gudden method of Brodal (1940)

Beside this method Allison (1953 a) applied the silver impregnation method of Glees (1946), just as Le Gros Clark and Meyer (1947) did in the rabbit, Meyer and Allison (1949) in Macaca mulatta and Papio papio, and Adey (1953) in Trichosurus vulpecula

The silver staining methods of Nauta (1950, 1957) and of Nauta and Gygax (1954) were applied by Johnson (1959) in the guinea pig, by Lammers (1959) in the cat, by Lohman and Lammers (1961) in the guinea pig and the cat, by Cragg (1961) in the rabbit, rat and cat, and by Sanders-Woudstra (1961) and White (1962) in the rat

Findings after extirpation of the olfactory bulb

Whereas Gudden (1870), Ganser (1882), Loewenthal (1897), van Gehuchten (1904), Winkler (1917), Young (1941, 1942), Morin (1950), Lohman and Lammers (1961), and White (1962) could only observe degeneration in the lateral olfactory tract after lesions which were confined to the olfactory bulb, Probst (1901) and Cajal (1901, 1911) reported also degenerated fibres in the anterior limb of the anterior commissure after ablation of the olfactory bulb

Also Fox and Schmitz (1943) could observe degenerated fibres in the anterior commissure after bulbar lesions They were of the opinion, however, that these fibres probably arise from the gyrus olfactorius communis, because they thought it very difficult to destroy any sizeable portion of the olfactory bulb without involving some of the anterior olfactory nucleus

After unilateral resections of the olfactory bulb in various mammals by Le Gros Clark and Meyer (1947), Adey (1953), Johnson (1959) and Lammers (1959) and after severing the olfactory peduncle in the monkey by Meyer and Allison (1949), terminal and preterminal degeneration could not only be observed by these authors in the area of distribution of the lateral olfactory tract, but also bilaterally in the bed nucleus of the stria terminalis and in the central amygdaloid nucleus

Both these nuclei are said to communicate with the olfactory bulb by way of the anterior commissure, because after unilateral leucotomy of the frontal lobe, in which experiment the lesion involved the fibres of the anterior commissure on the operated side but left the lateral olfactory tract intact, a similar result was obtained (Le Gros Clark and Meyer) In the Glees

preparations, however, the degeneration in the anterior commissure itself was either very slight (Le Gros Clark and Meyer, Adey) or not with certainty demonstrable (Meyer and Allison) In a recent publication Cragg (1961) reports degenerated fibres in the anterior limb of the anterior commissure of the rabbit, rat and cat after lesions at the posterior end of the olfactory bulb However, as this author mentions that the lesions also destroyed the majority of the efferent fibres in the anterior limb of the anterior commissure, it may be reasonably assumed that the anterior part of the anterior olfactory nucleus was also involved

Morin (1950) reported that no degeneration could be observed in the medial forebrain bundle after lesions of the olfactory bulb or peduncle

The question whether the septal area receives direct afferent connections from the olfactory bulb is answered in the negative by Probst (1901), Young (1941), Le Gros Clark and Meyer (1947), Meyer and Allison (1949), Adey (1953), and Lohman and Lammers (1961) After transection of the monkey olfactory peduncle Meyer and Allison could only trace degenerated fibres medial in the peduncle as far caudally as the superficial layer of the anterior hippocampal nucleus

Most authors found no degeneration in the hippocampal formation after bulbar ablation (Le Gros Clark and Meyer, Adey, Lohman and Lammers) or transection of the olfactory peduncle (Meyer and Allison) However, after unilateral bulbar and retrobulbar lesions Lammers (1959) observed in the cat degenerative fibres bilaterally in the extreme rostroventral tip of the hippocampus, where the gyrus dentatus grades over into the cortical amygdaloid nucleus Also Loewenthal (1897) reported bilateral degeneration in the Ammon's horn after resection of the olfactory bulb and anterior part of the olfactory peduncle of the rabbit

Tractus olfactorius lateralis

All investigators, who did experimental work in this field, are of the opinion that the lateral olfactory tract has its main origin in the olfactory bulb There is, however, no agreement about the question whether the fibres of this bundle arise from the mitral as well as from the tufted cells

From findings in preparations of new-born mice Cajal (1901, 1911) came to the conclusion that the axons of the tufted cells do not enter the lateral olfactay tract, but form part of the anterior limb of the anterior commissure

In accordance with this view are the findings of Winkler (1918) A few months after transection of the lateral olfactory tract in new-born rabbits only the mitral cells in the olfactory bulb exhibited different stages of total or partly pyknomorphy It is interesting to know that the author adds to this "They don't betake themselves as if their axons were immediately cut off" No trace of any atrophy could be observed in the "cellules empanachées médianes et inférieures"

After a similar transection Allison (1953 a) and Johnson (1959) could also observe retrograde changes in the mitral cells of the olfactory bulb only On account of quantitative data about the number of mitral cells and of the fibres in the lateral olfactory tract in 3 to 4 months old rabbits, Allison and Warwick (1949) already assumed before that only the axons of the mitral cells and not those of the tufted cells participate in the formation of the lateral olfactory tract

Only the experiments of Allison (1953 a) and those of Johnson (1959) provide data about a probable participation of the axons of the tufted cells of the accessory olfactory bulb in the formation of the lateral olfactory tract. The former author observed that after transection of this fibre bundle retrograde changes occur in the tufted cells of the accessory bulb. After a similar experiment Johnson could trace degenerating fibres from the stratum mitrale of the accessory olfactory bulb into the lateral olfactory tract.

As to the problem whether the lateral olfactory tract contains only fibres that arise from the bulbar area, we quote Loewenthal (1897), who after resection of the olfactory bulb and the tip of the anterior olfactory lobe in a rabbit reports: "Der Tractus lateralis erhalt, wie es scheint, aus Zellen des Lobus keinen wesentlichen Zuwachs mehr". Winkler (1918) reports that after extirpation of the olfactory bulb not a single fibre of the lateral olfactory tract remained intact. In contrast with this Le Gros Clark and Meyer (1947) are of the opinion that the medial part of the tract does not entirely consists of fibres which have their origin in the olfactory bulb. Seven days after unilateral extirpation of the olfactory bulb in the rabbit not all the fibres of the lateral olfactory tract situated medial to the endorhinal fissure were undergoing degeneration, whereas in the lateral part of the tract covering the piriform cortex almost all the fibres were degenerating.

Does the lateral olfactory tract contain bulbopetal fibres as well? Allison (1953 a) reports that two months after transection of the lateral olfactory tract the axons on the bulbar side of the lesion exhibited very little difference from those on the normal side. Johnson (1959) and Sanders-Woudstra (1961), however, were able to follow degenerated fibres into the bulb after a similar experiment Worth mentioning is that Fox, Fisher and Desalva (1948) report that in Macaca mulatta the medial fascicle of the anterior limb of the anterior commissure joins the lateral olfactory tract rostral to the olfactory tubercle and thus reaches the olfactory bulb

All authors consider the prepiriform and periamygdaloid cortex as the most important area that the lateral olfactory tract directly or by way of collaterals provides for. The most detailed data about the termination of the lateral olfactory tract in these cortices are furnished by the experiments of Le Gros Clark and Meyer (1947). After unilateral extirpation of the olfactory bulb in the rabbit degeneration was found to be most severe in the most superficial layer and, to a lesser degree, in the superficial zone of the plexiform layer. Very few fibres were seen penetrating deeply into the plexiform layer and they seemed hardly ever to reach the pyramidal cell layer. Thus it appears that the synapses here are practically entirely axo-dendritic, as Cajal had previously affirmed in preparations of normal mice.

According to Johnson (1959) the fibres leave the lateral olfactory tract from lateral to medial, so that at caudal levels only the medial fibres in the tract remain to terminate. Adey (1953) reports that in the periamygdaloid cortex near the amygdaloid fissure the degeneration extends more deeply through the pyramidal cell layer Loewenthal (1897) could only observe degeneration beneath the pyramidal cell layer of the periamygdaloid cortex and that bilaterally, when, together with the olfactory bulb, the rostral part of the anterior olfactory nucleus had been severed.

Winkler (1918) draws the attention to the changes which the pyramidal cells of the

prepiriform and periamygdaloid cortex undergo after extirpation of the olfactory bulb In Nissl preparations the cells take an intensive homogeneous deep blue colour, their dendrites are thin and darkly stained, they are in pyknomorph endstadia of altered cells Allison (1954), too, found a definite shrinkage and pyknosis of the pyramidal cells of the prepiriform area in a 52 year old man whose olfactory peduncle had been severed two years before The cell bodies were so deeply stained that their nuclei were invisible On the other hand, even after survival times of 310 days Jones and Thomasch (1962) were unable to observe a reduction in the number of pyramidal neurons of the rat prepiriform cortex after bulbar resection They were able to establish however, using the Golgi-Cox method a decrease in the number of dendritic branches arising from each pyramidal cell, most marked among dendritic branches of the higher orders without any obvious reduction in the number of primary dendrites

Elliot Smith (1909) and Sonntag and Woollard (1925) could see, with the naked eye, fibres running from the lateral olfactory tract to the olfactory tubercle in Orycteropus Besides, after extirpation of the rostral part of the olfactory bulb in Perameles, Elliot Smith could observe degenerated fibres running over the lateral part of the tubercle
Also in man Allison (1954) could trace a distinct fascicle of fibres from the medial side of the lateral olfactory tract to the plexiform layer of the olfactory tubercle These fibres constitute the "medial olfactory stria" or "medial olfacto-frontal fascicle" The observations of Elliot Smith are combatted by Edinger (1911) It is true that in normal brains of Orycteropus the medial part of the lateral olfactory tract covers part of the olfactory tubercle, but apart perhaps a few small fibres, all fibres of the tract terminate in the cortex of the olfactory lobe According to Edinger this is also the case in experimental material "Ich habe seit Jahren Hunden Kaninchen, Ratten und Mausen wiederholt den Lobus olfactorius abgeschnitten und die Degeneration der Tractus olfactorii kaudalwarts verfolgt Sie uberzieht sehr oft so wie es Elliot Smith abbildet, laterale Teile des Lobus parolfactorius, aber man sieht nur hochst selten ein oder das andere Faserchen eindringen, so selten, dass ich vermute, es handelt sich hier nur um abgesprengte durchziehende Faserchen, wie denn die ganze ubrige Fasermasse immer degeneriert bis in die kaudalsten Abschnitte des Lobus olfactorius zu verfolgen ist" In contradiction with Ioo (1931), who found that in the opossum many fibres of the lateral olfactory tract terminate in the olfactory tubercle, Cajal (1955) reports "In Marchi preparations it is impossible to find degenerated fibres in the plexiform zone after extirpation of the olfactory bulb '
The findings of Le Gros Clark and Meyer (1947), Meyer and Allison (1949), Adey (1953), Johnson (1959), Lammers (1959) and Sanders-Woudstra (1961) are in contradiction with this The former authors, for instance, found terminal degeneration in the plexiform layer of the tubercle and, in a few instances, around nerve cells and within the islands of Calleja, mainly in the lateral and ventral part The degeneration diminishes and gradually disappears as the posterior and medial sectors are approached

Degeneration was also established by these authors in the anterior olfactory nucleus, in the Glees preparations however only in the pars externa of this nucleus Kreiner (1937) was unable to see fibres from the lateral olfactory tract penetrating the pars externa in his normal Weigert sections of the white rat

As to the termination of the lateral olfactory tract in the amygdaloid complex, Cajal (1955) is of the opinion that its fibres have no termination in the amygdaloid nucleus He adds to this, however "Nonetheless, in Marchi preparations it is possible to find the entrance of degenerated fibres into the amygdaloid nucleus after ablation of the bulb and olfactory lobule"

Sanders-Woudstra (1961) reports that the fibres of the lateral olfactory tract in the periamygdaloid cortex do run in the direction of the amygdaloid complex, but that after ablation of the olfactory bulb only very little, diffusely scattered, degeneration was found in this complex

After extirpation of the olfactory bulb Le Gros Clark and Meyer (1947) found terminal degeneration in the nucleus of the lateral olfactory tract, which nucleus Johnson (1957 a) takes to belong to the anterior amygdala group.

They also found terminal degeneration in the cortico-amygdaloid transition area and in the medial and cortical amygdaloid nuclei In the latter nucleus only axo-dendritic synapses are alleged to occur This observation is confirmed by Meyer and Allison (1949) and Adey (1953) using the Glees method, and by Johnson (1959) and Lammers (1959), who made use of the Nauta method.

Adey reports also degeneration in the superficial parts of the heterolateral medial and cortical amygdaloid nuclei, while Lammers reports bilateral degeneration in the basal nucleus

No investigator mentions a termination of the lateral olfactory tract in the entorhinal cortex Whether there is degeneration in the hippocampus after bulbar ablation or not, has already come up for discussion before.

Anterior commissure

In most mammals three portions of the anterior commissure can be distinguished (Ariens Kappers et al., 1936, Kreiner, 1936)

1 pars olfactoria s bulbaris
2 pars interhemispherica
3 pars ad striam terminalem

The nineteenth century authors Luys (1865) and Meynert (1867) were of the opinion that fibres of the pars olfactoria might join the heterolateral pars interhemispherica across the midline, and vice versa

Luys describes this as follows: "Un portion de fibres convergentes olfactives s'entrecroissent sur la ligne médiane, parallèle aux fibres de la commissure blanche antérieure, aux-dessous desquelles elles sont situées et avec lesquelles elles sont souvent confondues et vont se distribuer vraisemblement dans la substance grise ganglionnaire, du côte opposé à celui d'on elles proviennent".

As early as 1870 Gudden could not agree with this "Sich kreuzende Fasern, wie sie Meynert in der Commissur des Menschen annimmt, habe ich beim Kaninchen nicht constatiren konnen, sammtliche Fasern der einen Seite gehen vielmehr allem Anscheine nach continuirlich in die der andern uber"

The observations of Le Gros Clark and Meyer (1947) confirmed by Meyer and Allison (1949), Adey (1953) Lammers (1959) and Johnson (1959) that after unilateral extirpation of the olfactory bulb not only terminal and preterminal degeneration is present in the area of distribution of the lateral olfactory tract but also bilaterally in the bed nucleus of the stria terminalis and the central amygdaloid nucleus, made these authors assume that these latter nuclei would communicate with the olfactory bulb by way of the anterior commissure

There is considerable variety of opinion among the investigators in this field about the origin and termination of the fibres of the anterior commissure Discussing this we shall mainly confine ourselves to the anterior limb (pars olfactoria) since this portion of the commissure may be considered to be the main connection between the anterior olfactory lobes on the right and left sides

In the guinea pig the anterior limb is considerably more developed and more deeply myelinated than the two other components of the anterior commissure It runs bilaterally after its crossing the midline with a laterally directed bend in rostral direction towards the olfactory bulb

It has always been a point of controversy whether the anterior commissure receives fibres from the olfactory bulb itself or not As early as 1882 Ganser established that after extirpation of only the olfactory bulb in the rabbit the pars olfactoria of the commissure remained unimpaired

Winkler (1917), Young (1941) Morin (1950), and Lohman and Lammers (1961) arrived at the same conclusion in various mammals

Loewenthal (1897) and van Gehuchten (1904) only observed degenerated fibres in the anterior commissure when both the olfactory bulb and the olfactory peduncle were injured The fibres could be traced to the heterolateral bulb According to Loewenthal part of these fibres terminates in the anterior olfactory lobe

Also Young (1942) was of the opinion that the interbulbar fibres arise from the anterior olfactory nucleus In the experiments of Lohman and Lammers (1961) the anterior commissure only exhibited degeneration when the lesion included the rostral part of the anterior olfactory nucleus The degenerated fibres could be followed into the pars externa of the heterolateral anterior olfactory nucleus

Brodal (1948) and Allison (1953 a) have tried to map out the origin of the fibres of the anterior commissure by use of the modified Gudden method (Brodal, 1940) Five to eight days after transection of this fibre bundle in the white rat the former author observed retrograde cell changes in the dorsal part of the anterior olfactory nucleus, the olfactory tubercle, the bed nucleus of the stria terminalis and the nucleus of the lateral olfactory tract Moreover, in the medial and cortical amygdaloid nuclei in some cells of the small-celled part of the basal amygdaloid nucleus in the anterior amygdaloid area, the cortico-amygdaloid transition area and the prepiriform, periamygdaloid and entorhinal cortex In the neopallial cortex, too did retrograde cell degeneration occur, mainly in the posterior and ventral areas Allison could not only observe cell degeneration in the pars dorsalis of the anterior olfactory nucleus but also in the tufted cells of the olfactory bulb, and from this the author concludes "From the retrograde degeneration in the tufted cells it may be concluded, that some, at

least, of the cells project into the anterior limb of the anterior commissure The same view was already held by Cajal (1901, 1911) on account of his findings in preparations of normal new-born mice After lesions of the anterior commissure Johnson (1959) observed fibre degeneration homolaterally in the tufted cell layer of the olfactory bulb and in the pars dorsalis of the anterior olfactory nucleus

In contrast with the findings of Ganser (1882), Loewenthal (1897) and van Gehuchten (1904) and in accordance with those of Probst (1901) Cajal (1901, 1911) reports that in his Marchi preparations of the rabbit after ablation of the anterior part of the olfactory bulb degenerated fibres are present in the anterior limb of the anterior commissure, which could be followed to the granular cell layer of the heterolateral olfactory bulb

Also Le Gros Clark and Meyer (1947) could trace degenerative fibres in the anterior limb of the anterior commissure after bulbar ablation The degeneration in the decussation of the commissure, however, was very slight, but more extensive, when also the rostral part of the anterior olfactory nucleus had been severed In the heterolateral bulb terminal degeneration was found in the granular cell layer, while a few fibres could be followed as far as among the glomeruli

A similar degeneration in the opposite bulb after unilateral bulbar extirpation is reported by Adey (1953) and Lammers (1959), while Adey found terminal degeneration in the pars dorsalis of the opposite anterior olfactory nucleus as well

Injury to, or transection of the anterior commissure is another method to determine the termination of the fibres of this bundle Fox and Schmitz (1942) reported that after interruption of the anterior commissure in the midline in young and adult cats, degenerated fibres could be traced into both olfactory and accessory olfactory bulbs Whether these were truly interbulbar fibres, the position of the lesion permitted no conclusions In later experiments, in which the lesions interrupted the commissure near the region of its crossing the midline of the cerebral hemisphere (Fox and Schmitz, 1943) it was found that the anterior limb of the anterior commissure distributes fibres to the olfactory bulb, the anterior olfactory nucleus, the anterior part of the piriform cortex and perhaps also to the olfactory tubercle and the accessory olfactory bulb

This last experiment was repeated by Fox, Fisher and Desalva (1948) in Macaca mulatta In normal preparations of this animal the small anterior limb of the commissure separates immediately after its decussation into three smaller strands After a short swing, lateroinferiorly from the posterior limb of the anterior commissure, the three strands turn sharply forward and course between the striatum and the olfactory tubercle in the striotubercular fusion In the Marchi preparations the granules in the medial strand suddenly become finer and in the intermediate and lateral strands they disappear completely At the level of the rostral end of the olfactory tubercle these strands themselves have disappeared as well

The medial strand however, courses through the inferior portion of the caudate nucleus into the lateral olfactory tract, and from here into the olfactory bulb

According to the authors the diminution of Marchi granules, as the medial fascicle courses through the region of the anterior olfactory nucleus, indicates that connections are made with this nucleus Thus, the anterior limb of the anterior commissure of the monkey distri-

butes by way of its three fascicles to the olfactory tubercle, the anterior olfactory nucleus and the olfactory bulb

After transection of the anterior limb of the anterior commissure just behind one olfactory bulb Allison (1953 a) observed terminal degeneration in the opposite bulb, mainly in the periventricular and granular cell layers This degeneration, however, was very much more severe in the homolateral olfactory bulb and extended outward to the external plexiform layer From this the author concludes that the bulbopetal fibres arise from basal areas of the hemisphere on the same side, as well as from the opposite olfactory bulb

These experiments might not entirely exclude the possibility that the retrobulbar area of one side contributes fibres through the anterior limb of the anterior commissure to the opposite olfactory bulb or retrobulbar area According to Allison this is, however, improbable, because in experiments, in which the anterior limb of the commissure was cut just behind the olfactory bulb and 2 mm further back, respectively, the resulting degeneration in the opposite olfactory bulb was not appreciably different in the two cases

In one experiment, in which the anterior limb was cut a little distance behind the anterior olfactory nucleus, terminal degeneration was found in the heterolateral anterior nucleus These findings of Allison were confirmed in the albino rat by Sanders-Woudstra (1961)

Lammers (1959), too, reports that after retrobulbar lesions the number of degenerated fibres in the homolateral olfactory bulb is much larger than in the heterolateral one

Finally it must be noted that, after lesions of the anterior commissure in the guinea pig at the level of the caudal part of the olfactory peduncle, Johnson (1959) could trace degenerative fibres to the homolateral prepiriform and piriform cortex and olfactory tubercle, while bilaterally terminal degeneration was present in the bed nuclei of the anterior commissure and stria terminalis and in the central amygdaloid nucleus In the heterolateral olfactory bulb degenerative fibres could be traced into the granular cell layer No degeneration could be established by Johnson in the heterolateral anterior olfactory nucleus

Medial forebrain bundle

In the literature are to be found only a few data about a probable participation of the medial forebrain bundle in the projection of the olfactory bulb and anterior olfactory nucleus

From their investigations of normal brains Herrick (1924) and Loo (1931) were of the opinion that fibres of the olfactory bulb as well as from the anterior olfactory nucleus form part of the medial forebrain bundle

Neither Morin (1950) in the guinea pig nor Sanders-Woudstra (1961) in the albino rat were able to confirm this experimentally

Interesting in the light of our own findings after injuring the pars medialis of the anterior olfactory nucleus is the account of the medial forebrain bundle given by Young (1936), based on a study of Weigert preparations of the normal guinea pig brain "From the pars medialis of the anterior olfactory nucleus fibres arise and course caudally in the ventromedial part of the crus to enter the medial forebrain bundle They form the medial olfacto-hypothalamic tract, which is the most rostral component of the bundle Whether or not fibres from the olfactory formation accompany these fascicles in rodents, as Herrick (1924) thought

to be the case in opossum, is uncertain; at least they are not demonstrable in the material available".

Observations

Lesions in the main and accessory olfactory formations

In 20 guinea pigs (Series B 1-B 20) lesions were made in the bulbar area, which were confined strictly to the main or accessory olfactory formation (for 6 of these lesions see figs. 47 and 48). In these cases degenerated fibres can be traced caudalward from the lesion into the lateral olfactory tract only. Neither in the anterior limb of the anterior commissure, nor medially or ventrally in the olfactory peduncle fibre degeneration can be observed. If the lesion is situated in the main olfactory formation, the degenerated fibres on their way to the laterally situated olfactory tract run through and beneath the accessory bulb. In this bundle the fibres reach as far as the margin of the entorhinal cortex.

Preterminal degeneration is found subjacent to the lateral olfactory tract and its collaterals in the following areas: between the olfactory tract and the pars externa of the anterior olfactory nucleus and among the superficial cells of this cell group, in the plexiform layer of the nucleus olfactorius anterior pars lateralis and of the prepiriform cortex, mainly confined to its superficial part (fig. 53). In the deeper part of this layer a variable number of degene-

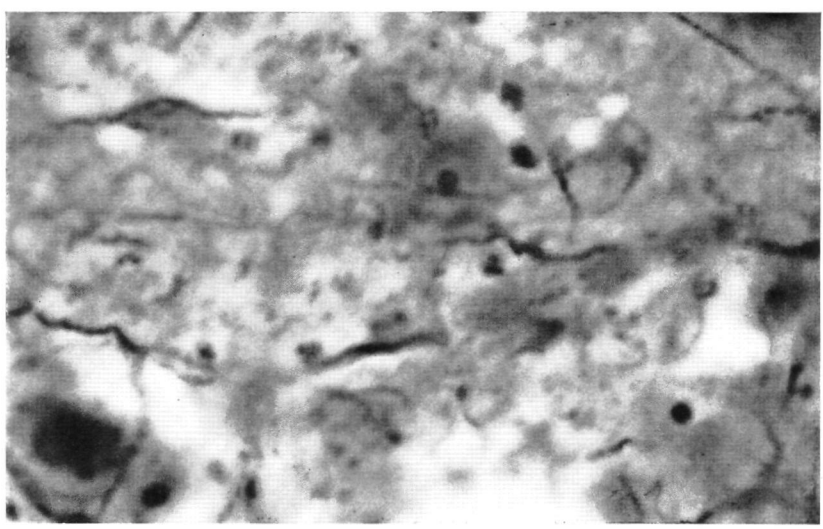


Fig. 53. Preterminal degeneration in the plexiform layer of the prepiriform cortex following ablation of the olfactory bulb. Nauta method (1950). Magnification 2500 x

rated fibres can be observed running obliquely from the lateral olfactory tract into the pyramidal cell layer. Further, degeneration is found superficially in the plexiform layer of the

lateral part of the olfactory tubercle and among the superficial cells of the islands of small neurons, most intensively rostrally in the tubercle and decreasing caudally

Degenerating preterminals are also present in the plexiform layer of the anterior amygdaloid area and of the nucleus of the lateral olfactory tract, almost exclusively in its superficial part In one experiment degenerated fibres can be followed from the olfactory bundle into the rostral tip of the nucleus of the lateral olfactory tract

In the periamygdaloid cortex the degeneration is found to be most severe superficially in the plexiform layer, but degeneration is also found deeper in this layer as far as among the superficial cells of the pyramidal cell layer As regards the termination of the lateral olfactory tract in the amygdaloid complex we can only observe degeneration in the plexiform layer of the cortico-amygdaloid transition area and of the anterolateral part of the cortical amygdaloid nucleus and among the superficial cells thereof Here, however, the degeneration is less severe than in the periamygdaloid cortex

Probably due to the smallness of some lesions and the vagaries of silver staining it is not possible to find the preterminal degeneration, described above, in all guinea pig brains in which bulbar lesions are made Especially more caudally in the area of distribution of the lateral olfactory tract e g in the area amygdaloidea anterior, the periamygdaloid cortex and the amygdaloid complex the degeneration in many brains is either very slight or totally absent

Le Gros Clark (1950-1957) reports a topical localization in the projection of the olfactory epithelium to the olfactory bulb in the sense that certain local areas of the olfactory epithelium are projected to local regions of the bulb As to the problem whether a such-like organization exists in the projection of the olfactory bulb to the tertiary olfactory centers of the guinea pig brain it must be noted that this could not be examined by us on account of the too little diversity in the size and position of the bulbar lesions and the characteristic capriciousness of silver impregnation

Further, it could not be examined wheter the accessory olfactory bulb projects to an apart region in the area that the lateral olfactory tract provides for, because in our experiments lesions in the accessory bulb always at the same time interrupted fibres running from the main olfactory bulb on their way to the lateral olfactory tract

It is of importance to note that in none of the operated guinea pigs degenerating fibres or preterminals could be found in the septal nuclei, the bed nucleus of the stria terminalis, the central, basal, lateral and medial amygdaloid nuclei and the hippocampus, both homo- and heterolaterally

Lesions in the anterior olfactory nucleus

When lesions in the bulbar area also comprise one of the cell groups of the nucleus olfactorius anterior pars rostralis or the entire *pars rostralis*, as is the case in the guinea pigs R 1-R 5 (for 3 of these lesions see fig 49), degenerated fibres are to be found not only in the lateral olfactory tract but also in the anterior limb of the anterior commissure

The projection via the lateral olfactory tract is similar to that described after strictly bulbar lesions The degenerated fibres in the anterior commissure can be traced to the heterolateral olfactory peduncle where they distribute to the pars externa of the anterior olfactory nucleus

None can be followed into the olfactory bulb Further no degenerated fibres of the anterior limb can be seen crossing to the pars posterior or the pars ad striam terminalem of the anterior commissure

In the guinea pigs R 1-R 4 the pars externa, in which the degenerated fibres terminate, seems to contain a smaller number of cells than the cell group on the operated side Besides, of the remaining cells some are shrunken or show chromatolytic changes

In the guinea pigs D 1-D 3 the lesion is localized in the *pars dorsalis* of the anterior olfactory nucleus (for 1 of these lesions see fig 50) In these cases degenerated fibres can be traced caudalward from the lesion via the anterior commissure to the heterolateral bulbar area, where they obviously end in the granular cell layers of the main and accessory olfactory bulbs Degenerated fibres can also be seen running rostralward from the lesion into the homolateral olfactory bulb Whether these are interrupted fibres of the anterior commissure only, or the anterior olfactory nucleus itself also issues fibres to the olfactory bulb, could not be decided That the number of degenerated fibres after retrobulbar lesions is notably larger in the homolateral bulb than in the heterolateral one, as described by Allison (1953 a) and Lammers (1959), could not be ascertained by us in our preparations

Unlike the cases D 1 and D 3 the lateral olfactory tract in guinea pig D 2, in which the lesion is restricted to the pars dorsalis, proved to contain no degenerated fibres This suggests that this part of the anterior olfactory nucleus does not issue fibres to the olfactory bundle

Whereas in guinea pig D 1 the preterminal degeneration in the area of distribution of the lateral olfactory tract is the same as in cases with strictly bulbar lesions, in guinea pig D 3, in which the lesion involves the rostral part of the nucleus olfactorius anterior pars lateralis and probably also the pars externa, degeneration in the periamygdaloid cortex is found not only in the plexiform but also in the polymorph layer

This same degeneration in the polymorph layer of the periamygdaloid cortex is found in the guinea pigs L 1 and L 2 In these cases the lesion also destroys the *pars externa* and the rostral part of the nucleus olfactorius anterior *pars lateralis* but does not involve the pars dorsalis of this nucleus In the horizontal sections of these two brains degenerated fibres are found in the lateral olfactory tract, in the anterior limb of the anterior commissure and in the polymorph layer of the homolateral nucleus olfactorius anterior pars lateralis These latter fibres can in this layer be followed caudalward, but not farther than the olfactory tubercle They appear to turn in a lateroventral direction and to reach the lateral olfactory tract between the pars lateralis and the pars ventralis of the anterior nucleus This could not determined accurately in the horizontal sections of these animals However, the more widespread degeneration in the periamygdaloid cortex in these cases, compared with the degeneration after strictly bulbar lesions, is in conformity with this course of the degenerated fibres This finding agrees with Cragg's (1961) observation in the rabbit, rat and cat of degenerated fibres leaving the anterior limb of the anterior commissure diffusely in a postero-ventral-lateral direction and passing into the deeper layers of pyramidal neurons in the prepiriform cortex and olfactory tubercle after lesions at the posterior end of the olfactory bulb in which, very probably, also the anterior part of the anterior olfactory nucleus was destroyed

It could not be decided with certainty whether these fibres arise from the rostral part

of the pars lateralis from the pars externa or from both cell groups, although it appears likely in view of the position of the lesion in guinea pig D 3 (fig 50) that the fibres have their main origin in the rostral part of the pars lateralis

The lesion in the guinea pigs L 1 and L 2 also interrupts the fibres of the anterior commissure which have their origin in the pars rostralis of the anterior olfactory nucleus These fibres can be traced caudalward from the lesion in the anterior commissure to the opposite pars externa, which cell group in guinea pig L 1 appears to show a partial loss of cells However, no comparison could be made with the destroyed homolateral cell group

Finally a lesion was made in the caudal part of the nucleus olfactorius anterior *pars medialis* (guinea pig M 1) Medially and ventrally in the olfactory peduncle degenerated fibres can be traced rostralward from the lesion as far as the rostral end of the peduncle It could not be decided whether these fibres enter the olfactory bulb or not, because the relatively small number of degenerated fibres which possibly enter the bulbar area are to be lost among the normal fibres of the bulbar granular layer As indicated by the data of the experiments O 1, O 2, O 6 and O 7 these fibres have their origin in more caudally situated basal areas of the hemisphere It appears doubtful that they arise from the septal area, because in the two guinea pigs O 8 and O 9 in which septal lesions have been produced (for 1 of these lesions see fig 52), we were unable to trace degenerated fibres into the olfactory peduncle

The degeneration in guinea pig M 1 which extends medially and ventrally in the peduncle caudalward from the lesion as far as the caudal end of the pars medialis, is very likely a retrograde one

Also the medial forebrain bundle, which runs ventromedially in the olfactory peduncle, is interrupted by the lesion Rostral to the lesion the degenerated fibres of this bundle appear to distribute mainly to the pars medialis, while some fibres can be traced to the pars dorsalis Caudalward from the lesion the degenerating slender fascicles of the medial forebrain bundle are fanning out in the olfactory tubercle and can be followed through the diagonal band of Broca to the lateral hypothalamic area

Lesions elsewhere in the anterior olfactory lobe

The foregoing experiments R 1-R 5 and D 1-D 3 have demonstrated the existence of two major pathways in the anterior commissure which have their origin in the pars rostralis and in the pars dorsalis of the anterior olfactory nucleus and project to the opposite nucleus olfactorius anterior pars externa and to the olfactory bulb respectively For confirming these projections we have transected and injured the *anterior limb of the anterior commissure* behind the olfactory peduncle in the guinea pigs O 1-O 3 (for one of these lesions see fig 51) In all three cases degenerated fibres can be traced from the lesion via the anterior commissure to the nucleus olfactorius anterior pars externa and the granular cell layers of the main and accessory olfactory formations both homo- and heterolaterally The paucity of cells in the partes externae is once more conspicious No retrograde cell changes could be detected in the mitral and tufted cells of the olfactory bulb and in the pars rostralis and pars dorsalis of the anterior olfactory nucleus

In the guinea pigs O 1 and 0 2 the lesion extends ventrally into the *olfactory tubercle* In

both animals degenerated fibres can be traced ventral to the anterior limb of the anterior commissure rostralward into the olfactory peduncle In guinea pig O 1 these fibres are found in the fascicles of the medial forebrain bundle as well as medially and ventrally in the peduncle, where they can be followed as far as the olfactory bulb In guinea pig O 2, in which the lesion is situated more laterally in the olfactory tubercle degenerated fibres run only to the ventral side of the peduncle

The same degeneration as in the preceding cases can be observed in the guinea pigs O 6 and O 7 In the guinea pig O 6 a lesion has destroyed part of the prepiriform cortex and the anterolateral part of the olfactory tubercle From the lesion degenerated fibres run ventral to the anterior limb of the anterior commissure medialward in the plexiform layer between the nucleus accumbens and the rostral part of the olfactory tubercle, then turn slightly ventralward and course ventrally in the olfactory peduncle rostralward as far as the rostral end thereof In the experiment O 7 the lesion is situated more medially in the tubercle where it also interrupts the fibre bundles of the medial forebrain bundle Degenerated fascicles of this bundle extend into the olfactory peduncle as far as the pars medialis
In all four experiments the degeneration caudal to the lesions has not been examined

It could not be decided with certainty whether the *anterior olfactory nucleus pars lateralis* issues fibres to the anterior commissure or not After a small lesion at the transition from the pars lateralis to the prepiriform cortex (guinea pig O 5) no degenerated fibres could be traced to the heterolateral peduncle Also in guinea pig O 6 where the lesion is situated in the *prepiriform cortex* and in *the olfactory tubercle* lateral to the anterior limb of the anterior commissure this commissure was found to be entirely normal

Finally, it appears from the experiments O 4-O 6, in which the *lateral olfactory tract* has been interrupted that this fibre bundle does not contain bulbopetal fibres Caudalward from the lesion degenerated fibres can be traced as far as the margin of the entorhinal cortex, rostrally degeneration in the lateral olfactory tract is only present in the vicinity of the lesion

Conclusions and discussion

The most important result of our experiments in the guinea pig is that after lesions of the main and accessory olfactory formations degenerated fibres from the bulbar area can be traced into the lateral olfactory tract only This does not agree with the results of similar experiments in the rabbit and the phalanger as reported by Probst (1901), Cajal (1901, 1911) and more recently by Le Gros Clark and Meyer (1947) and Adey (1953)
Allison (1953 a b) stated that there exist two relatively independent pathways which relay olfactory impulses from the glomeruli a mitral cell-lateral olfactory tract system and a tufted cell-anterior commissure system The fibres of the lateral olfactory tract terminate in the superficial olfactory centers like the anterior olfactory nucleus the prepiriform and periamygdaloid cortex, the olfactory tubercle, the nucleus of the lateral olfactory tract and the corticomedial group of the amygdaloid complex The axons of the tufted cells terminate in centers that are situated more centrally like the central amygdaloid nucleus and the bed nucleus of the stria terminalis both homo- and heterolaterally and they also provide for the commissural connections between the olfactory bulbs

The existence of two systems of bulbofugal connections is founded by Allison on the observation in rabbits and rats that after transection of the lateral olfactory tract only retrograde cell changes occur in the mitral cells but not in the tufted cells of the olfactory bulb The latter would be the case if the anter or limb of the anterior commissure is injured as well In our opinion, however, the small number of tufted cells showing retrograde changes as well as the small intensity of these changes, which according to Allison is probably attributable to the well-developed collaterals of the tufted cell axons, give little support to this scheme of bulbar projections Besides, in recent physiological experiments Green et al (1962) and von Baumgarten et al (1962) showed that the rabbit mitral and tufted cells may be driven antidromically by stimulation of the lateral olfactory tract, whereas stimulation of the anterior commissure failed to produce antidromic activity of the tufted cell bodies

In the guinea pig the anterior commissure is found degenerated after bulbar lesions when the lesions are situated caudally in the olfactory bulb or at the transition from the bulbar to the retrobulbar area, in which cases the pars rostralis or pars dorsalis of the anterior olfactory nucleus are involved In none of our experiments we were able to demonstrate in the Nauta sections degeneration in the bed nucleus of the stria terminalis or in the central amygdaloid nucleus It is interesting to note that Cowan and Powell (1956) described a "terminal degeneration in Glees preparations from the septal, hypothalamic and preoptic regions, including the bed nucleus of the stria terminalis, of the normal monkey and man The fact that Adey et al (1958) failed to verify this finding in a large number of Glees, Nauta and Bodian sections once again stresses the vagaries of the silver impregnation methods and the differences in interpretation by various authors of the results obtained with these methods

Lateral olfactory tract

The lateral olfactory tract has its main origin in the olfactory bulb Because it is evident from our experiments that the anterior commissure does not receive fibres from the olfactory formation, one may assume that not only the mitral cells but also the tufted cells send their axons into the lateral olfactory tract (fig 54) We were unable to verify this experimentally utilizing the retrograde changes appearing in nerve cells after their axons have been cut, because in the adult guinea pigs O 4-O 6, in which the olfactory tract had been transected, the survival times were probably too short and the distance from the lesion to the perikarya too great for developing retrograde changes in the mitral and tufted cells of the olfactory bulb

The lateral olfactory tract distributes its fibres mainly to the prepiriform and periamygdaloid cortex Whereas in the prepiriform cortex the distribution of the degeneration is the same as described by Le Gros Clark and Meyer (1947) in the rabbit and by White (1962) in the rat, namely chiefly in the superficial part of the plexiform layer, the degeneration in the periamygdaloid cortex extends into the superficial cells of the pyramidal cell layer Thus it appears that the synaptic mechanism in this area is not entirely axo-dendritic

The distribution of the lateral olfactory tract to the olfactory tubercle, the anterior amygdaloid area and the nucleus of the lateral olfactory tract conforms generally to that noted by earlier investigators In contrast with Le Gros Clark and collaborators, who reported a bulbar projection only to the pars externa of the anterior olfactory nucleus the olfactory tract in the

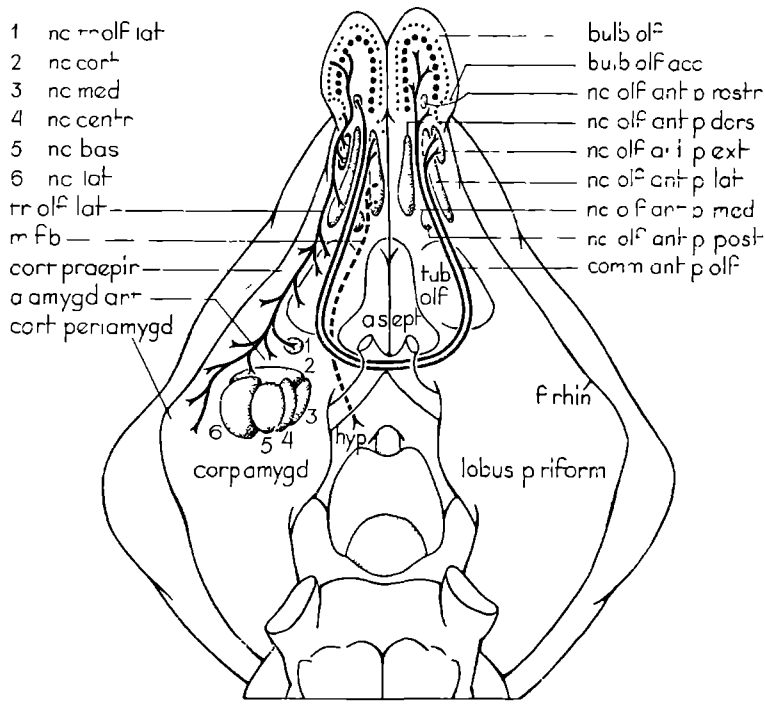


Fig 54 A diagram of the principal connections of the main and accessory olfactory bulb and of the anterior olfactory nucleus in the guinea pig

guinea pig distributes also to that portion of the pars lateralis which is not surrounded by the pars externa A termination of the olfactory bundle in the other portions of the anterior nucleus, particularly in the pars rostralis and pars dorsalis, could not be demonstrated
The most striking difference from the results of investigators using the Glees method, concerns the distribution of the fibres of the lateral olfactory tract to the amygdaloid complex In the Nauta sections of the guinea pig brain we were unable to confirm the rather extensive projection to the cortico-medial group of amygdaloid nuclei reported by these authors Whether this is due to interspecific variation or to the use of different silver impregnation methods, may be solved using the Nauta method in experiments on other mammals

It is evident from the observations in guinea pig B 8 that also the tufted cells of the accessory bulb contribute their axons to the lateral olfactory tract, while the findings from the experiments D 3, L 1 and L 2 indicate the existence of a third source of origin of fibres of the olfactory tract, which projects to the polymorph layer of the periamygdaloid cortex These fibres, which arise very likely from the rostral part of the nucleus olfactorius pars lateralis, run caudalward for some distance, but not farther than the olfactory tubercle, in the

polymorph layer of the pars lateralis turn in a latero-ventral direction between the pars lateralis and the pars ventralis of the anterior nucleus and thus reach the bulk of the lateral olfactory tract Via this pathway they continue their way to the periamygdaloid cortex, where they appear to reach their area of termination through the pyramidal cell layer
Finally it may be concluded from the experiments O 4-O 6 that the lateral olfactory tract of the guinea pig does not contain bulbopetal fibres

Anterior commissure

From our experiments it appears that in the pars olfactoria of the anterior commissure are represented two major projections from the anterior olfactory nucleus One such pathway originates in the pars rostralis and terminates in the pars externa of the heterolateral anterior nucleus the second forms a connection between the nucleus olfactorius anterior pars dorsalis on the one side and the granular cell layers of the main and accessory olfactory bulbs on the other side (fig 54)

In all experiments in which degenerated fibres of the anterior commissure could be traced to the pars externa this cell group seemed to contain less cells than the pars externa on the operated side Whether this is due either to a normal variability in the number of cells or to a cell loss as a result of retrograde or transneuronal atrophic changes is difficult to determine because more acute cellular changes such as chromatolysis are not striking Besides also in normal brains occasionally cells are met with which resemble retrograde changed ones (Brodal 1948)
Very probably the pars olfactoria of the anterior commissure receives no fibres from the pars medialis and the pars lateralis of the anterior olfactory nucleus the prepiriform cortex and the olfactory tubercle

The functional significance of the above mentioned pathways in the anterior commissure is by no means clear especially because so little is known about the afferent connections of the anterior olfactory nucleus Only Lammers and Lohman (1957) and Sanders-Woudstra (1961) provide data about afferent connections to the anterior nucleus from the homolateral basal areas of the cerebral hemisphere Sanders-Woudstra reports that in the albino rat a longitudinal association system is localized in the piriform cortex outside the external capsule The fibres of this system run parallel to the external capsule in anteroposterior direction and vice versa and probably into the anterior olfactory nucleus Lammers and Lohman could trace degenerated fibres by way of the external capsule to the nucleus olfactorius anterior pars posterior and pars dorsalis after lesions of the cat periamygdaloid cortex

Summarizing the results of our experiments we may state that in the guinea pig the following projections and pathways to the anterior nucleus exist the olfactory bulb projects via the lateral olfactory tract to the pars externa and the posterior part of the pars lateralis The opposite pars rostralis projects via the anterior commissure to the pars externa The medial forebrain bundle contains pedunculopetal fibres which distribute mainly to the pars medialis The origin of these fibres is unknown Also ventrally and medially in the olfactory peduncle pedunculopetal or bulbopetal fibres occur which can be followed rostralward as far

as the rostral end of the peduncle and probably extend into the olfactory bulb It appears that these fibres have their main origin in the olfactory tubercle

Medial forebrain bundle

The present findings agree with Young's observation in normal material of the guinea pig that the pars medialis of the nucleus olfactorius anterior projects by way of the medial forebrain bundle to the lateral hypothalamic area the medial olfacto-hypothalamic tract (fig 54)

No fibres could be traced into this pathway from the main and accessory olfactory bulb and from the nucleus olfactorius anterior pars rostralis, pars dorsalis and pars lateralis It could not be examined in our material whether the pars posterior and pars lateralis contribute fibres to the medial forebrain bundle or not

Beside pedunculofugal fibres the bundle contains pedunculopetal fibres which distribute mainly to the pars medialis The origin of the latter fibres is unknown

Summary

In the first part of the present study the nuclear configuration of the anterior olfactory lobe of the guinea pig (Cavia porcellus) has been described on the basis of serial sections of young and adult animals, stained with cresyl violet and by the Kluver-Barrera technique The description is supplemented with an atlas of serial drawings of frontal and horizontal sections of this area and with many photomicrographs of cells

The study was carried out to provide the anatomical basis for experimental work on the connections of the olfactory bulb and the anterior olfactory nucleus as described in the second part of our study

In the bulbar area the main and accessory olfactory bulbs are well developed Both formations have a typical mammalian structure The efferent cells of the main bulb are the mitral and tufted cells, while the role of the short-axon cells which are present in the granular and periventricular layers is not understood In the accessory bulb only tufted cells are present which resemble the internal tufted cells of the main bulb

The granular cell layer of the accessory olfactory formation is traversed by deeply myelinated fibres which pass from the dorsal side of the olfactory bulb to the lateral olfactory tract

The anterior olfactory nucleus can be divided topographically into a pars rostralis, dorsalis, lateralis, medialis, ventralis, posterior and a pars externa Certain differences in cell size and arrangement were identified between the various portions of the nucleus

The cell clusters of the pars rostralis are situated entirely intrabulbarly They are variable in number, size and position In some brains they are continuous with the rest of the anterior olfactory nucleus Also the rostral parts of the pars lateralis and pars dorsalis are lying inside the bulbar area Caudalward the anterior olfactory nucleus grades over dorsally into the neocortex, laterally into the prepiriform cortex, ventrally into the olfactory tubercle, and medially into the septal area and nucleus hippocampi anterior

The cortex piaepiriformis is well developed, showing four layers throughout its extent The regio praepyriformis lateralis of Rose is considered by us a transitional zone between the prepiriform cortex ventrally and the area insularis agranularis ventralis and posterior dorsally

The olfactory tubercle of the guinea pig is not quite so highly developed as in certain other mammals, for instance the cat It is least well differentiated in its anterior part Only in the posterior part of the tubercle the pyramidal and polymorph cell layers are distinguishable from one another A subdivision into lateral, intermediate and medial portions, as in other mammals has been done, could not be established in the guinea pig Emphasis has been laid on the conglomerations of small neurons in the lateral part of the tubercle

An area perforata anterior, as described in Orycteropus by Sonntag and Woollard, is not present in the guinea pig

The nucleus of the diagonal band of Broca is a caudal continuation of the medial septal nucleus and extends caudal to the olfactory tubercle as far as the prepiriform cortex

In the well developed area septalis the following nuclei were established nucleus hippocampi anterior, nucleus septohippocampalis, nucleus medialis septi, bed nucleus of the commissura fornicis, nucleus triangularis septi, bed nucleus of the commissura anterior, nucleus lateralis septi and nucleus septalis fimbrialis

Emphasis has been laid on the position and extension of the nucleus triangularis septi in the guinea pig In this animal it clearly differs from the bed nucleus of the commissura fornicis A division of the lateral septal nucleus into a dorsal and a ventral part, as described by Andy and Stephan, could not be made

The connections of the main and accessory olfactory bulb and of the anterior olfactory nucleus have been studied experimentally, using the Kluver-Barrera and the Nauta techniques to show degenerated fibres after surgical and electrolytic lesions The findings of these experiments may be summarized as follows

1 The lateral olfactory tract is the only projection bundle of the olfactory bulb and accessory olfactory bulb Fibres of this tract terminate in the pars externa and pars lateralis of the anterior olfactory nucleus, prepiriform cortex, lateral part of the olfactory tubercle, anterior amygdaloid area, nucleus of the lateral olfactory tract and periamygdaloid cortex

The area of distribution of the lateral olfactory tract in the amygdaloid complex is limited to the anterolateral part of the cortical nucleus

2 Very likely the rostral part of the nucleus olfactorius anterior pars lateralis projects via the lateral olfactory tract to the polymorph layer of the periamygdaloid cortex

3 By way of the anterior limb of the anterior commissure the pars rostralis of the anterior olfactory nucleus projects to the pars externa of the heterolateral anterior nucleus, the pars dorsalis to the heterolateral main and accessory olfactory bulbs

4 The pars medialis of the anterior olfactory nucleus is connected via the medial forebrain bundle with the lateral hypothalamic area. This fibre bundle also contains pedunculopetal fibres of unknown origin which distribute mainly to the pars medialis of the anterior nucleus

5 These experimental data about the connections of the anterior olfactory nucleus are in accordance with the topographical and histological differentiation of this nucleus

6 Ventrally and medially in the olfactory peduncle fibres are present which arise from more caudally situated basal areas of the hemisphere e g the olfactory tubercle Very probably these fibres extend into the olfactory bulb.

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stellingen

I

De commissura anterior van de cavia bevat geen echte commissurale vezels van de bulbus olfactorius en bulbus olfactorius accessorius

II

De door Cajal in de area septalis van de muis beschreven nucleus triangularis is gelijk te stellen aan de bed nucleus van de commissura hippocampi ventralis van de cavia

III

Het verdient aanbeveling na traumatische cervicale dwarslesies van het ruggemerg zo spoedig mogelijk te beginnen met passieve oefen- en electrotherapie van de benen

IV

Verschillen in ontwikkeling en hoeveelheid vruchtwater tussen de leden van een monochoriale eeneiige tweeling worden waarschijnlijk veroorzaakt door een zeer kleine asymmetrie in de derde circulatie van de placenta

V

De ambulante behandeling van de longtuberculose werkt het ontstaan van resistente stammen van het Mycobacterium tuberculosum in de hand

VI

De niet-metastatische veranderingen in cerebro bij carcinomen zijn nog onvoldoende verklaard